1   **Thalamocortical contribution to cognitive task activity**

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29 **Abstract**

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31 Thalamocortical interaction is a ubiquitous functional motif in the mammalian brain.

32 Previously (Hwang et al., 2021), we reported that lesions to network hubs in the human

33 thalamus are associated with multi-domain behavioral impairments in language,

34 memory, and executive functions. Here we show how task-evoked thalamic activity

35 and thalamocortical interactions are organized to support these broad cognitive abilities.

36 To address this question, we analyzed functional MRI data from human subjects that

37 performed 127 tasks encompassing a broad range of cognitive representations. We first

38 investigated the spatial organization of task-evoked activity and found that multi-task

39 thalamic activity converged onto a low-dimensional structure, through which a basis set

40 of activity patterns are evoked to support processing needs of each task. Specifically, the

41 anterior, medial, and posterior-medial thalamus exhibit hub-like activity profiles that

42 are suggestive of broad functional participation. These thalamic task hubs overlapped

43 with network hubs interlinking cortical systems. To further determine the cognitive

44 relevance of thalamocortical interactions, we built a data-driven thalamocortical

45 interaction model to test whether thalamocortical functional connectivity transformed

46 thalamic activity to cortical task activity. The thalamocortical model predicted task-

47 specific cortical activity patterns, and outperformed comparison models built on cortical,

48 hippocampal, and striatal regions. Simulated lesions to low-dimensional, multi-task

49 thalamic hub regions impaired task activity prediction. This simulation result was

50 further supported by profiles of neuropsychological impairments in human patients

51 with focal thalamic lesions. In summary, our results suggest a general organizational

52 principle of how thalamocortical interactions support cognitive task activity.

53

54 **Impact Statement:** Human thalamic activity transformed via thalamocortical functional

55 connectivity to support task representations across functional domains.

Introduction

Distributed neural activity supports a broad range of perceptual, motor, affective, and cognitive functions. Discovering how brain systems implement this broad behavioral repertoire is critical for elucidating the neural basis of human cognition. Past studies have revealed two organizational principles—low-dimensional architecture and multi-task hubs—that connect distributed neural activity with task performance across functional domains.

The application of dimensionality reduction techniques on whole-brain imaging data has revealed a relatively low-dimensional organization of distributed neural activity. Specifically, the number of variables required to explain a large amount of variance in distributed neural activity is far lower than the total number of variables in the data (MacDowell and Buschman, 2020; Nakai and Nishimoto, 2020; Shine et al., 2019a). The spatiotemporal patterns of these variables are commonly referred to as intrinsic networks in task-free conditions, or manifolds, motifs, and latent components in task contexts. This low-dimensional organization may reflect an elementary set of information processes implemented by distributed brain systems (Cunningham and Yu, 2014; Yeo et al., 2016), in which different tasks selectively engaged selective latent activity patterns depending on the specific processing requirements of individual tasks.

The anatomical overlap between spatiotemporal components predicts that some brain regions broadly participate in multiple tasks. In support of this prediction, studies have found that associative regions in frontal and parietal cortices are involved in executing a wide array of tasks (Cole et al., 2013; Duncan, 2010). These task-flexible regions, also commonly referred to as brain hubs (Gratton et al., 2018; van den Heuvel and Sporns, 2013), have diverging connectivity with multiple brain systems, and are thought to perform integrative functions that allow perceptual inputs to interact with contextual task representations for adaptive task control (Bertolero et al., 2018, 2015; Ito et al., 2022;

85   Nee, 2021). The behavioral significance of brain hubs is affirmed by lesion studies

86   demonstrating that lesions to hub regions are associated with task impairments across

87   multiple functional domains (Hwang et al., 2021; Reber et al., 2021; Warren et al., 2014).

88

89   However, a prevailing assumption is that diverse human behavior depends on the

90   organization of cortical activity, and the contribution from subcortical regions,

91   particularly the thalamus, is not well understood. Our previous studies demonstrated

92   that the human thalamus contains a complete representation of intrinsic cortical

93   functional networks, and additionally, exhibits a hub-like connectivity profile

94   interlinking multiple cortical systems (Hwang et al., 2021, 2017). Furthermore, lesions to

95   the anterior and the medial thalamus in human patients are associated with behavioral

96   impairments across functional domains (Hwang et al., 2020a, 2021). Given that every

97   cortical region receives projections from multiple thalamic nuclei and that the thalamus

98   mediates striatal and cerebellar influences on cortical processes (Jones, 2001; Sherman,

99   2007; Shine, 2020), thalamocortical interaction is ideally suited to shape cortex-wide

100 activity patterns that instantiate cognitive representations. Whether thalamic task

101 activity exhibits similar low-dimensional organization and how thalamocortical

102 interactions contributes to cognitive task activity remains unclear.

103

104 The goal of the current study was to determine how thalamic task-evoked activity, low-

105 dimensional organization, and thalamic hub architecture are organized to support

106 cognitive functions across diverse functional domains. To this end, we analyzed

107 functional magnetic resonance imaging (fMRI) data where human subjects performed a

108 rich battery of tasks designed to elicit neural activity for a wide range of cognitive

109 functions. Our study addressed the following three specific questions. First, does task-

110 evoked thalamic activity exhibit a low-dimensional organization? Second, are there

111 task-flexible thalamic hub regions that exhibit task-evoked responses across diverse task

112 domains? Third, can thalamic task-evoked activity transformed via thalamocortical

113 functional connectivity (FC) predict cortical task-evoked activity patterns? Answering

114   these three questions would reveal a general principle of how thalamocortical

115   interactions contribute to higher-order, multi-domain cognitive task activity for flexible

116   human behavior.

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Results

120   **Results**

121

122   To determine the organization of task-evoked thalamic activity and thalamocortical

123   interactions, we analyzed two publicly available fMRI datasets, both of which utilized

124   rich batteries of tasks designed to elicit a wide range of processes encompassing

125   perceptual, affective, memory, social, motor, language, and cognitive domains (Figure

126   1A). In the first dataset, the multi-domain task battery (MDTB) dataset, 21 subjects

127   performed 25 behavioral tasks (King et al., 2019). In the second dataset, the Nakai and

128   Nishimoto (N&N) dataset, 6 subjects performed 103 tasks (Nakai and Nishimoto, 2020).
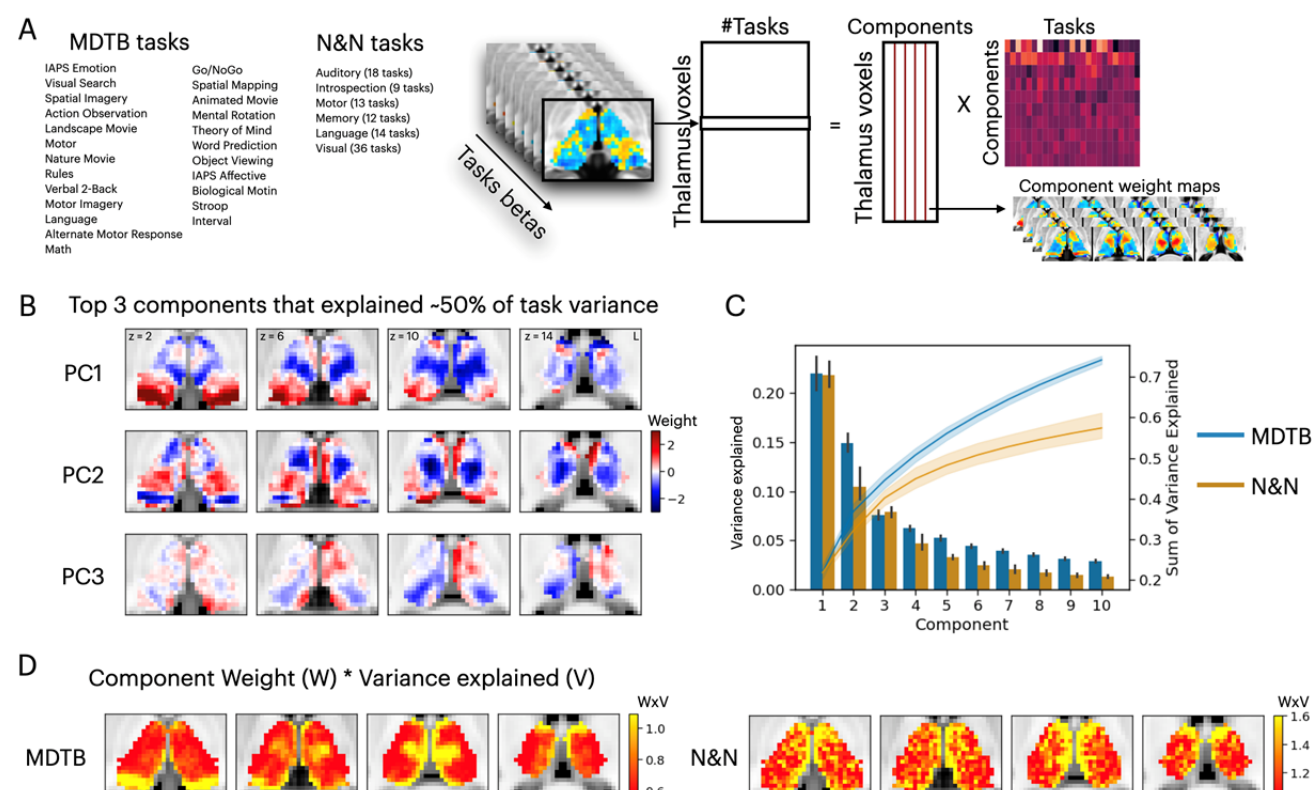

129

130   Figure 1 Low-dimensional organization of thalamic task-evoked response that supports

131   multi-task performance. (A) We decomposed the high-dimensional multi-task evoked

132   activity matrix into low-dimensional spatial components in the human thalamus and a

133   task-wide loading matrix. For a list of all tasks see Figure 1-Supplementary File 1 (B)

134   Spatial topography of the top three components from the MDTB dataset that explained

135   about 50% of the variance in the group averaged task activity matrix. For top

136   components for the N&N dataset see Figure 1-Figure Supplement 1. For the loadings

137   between tasks and components, see Figure 1-Figure Supplement 2. (C) Results from

138   applying PCA to single subjects. For both the MDTB and N&N datasets, for individual

139 subjects up to 60% of the variance across multiple tasks can be explained by the top 10
140 components. Error bars and shaded areas indicate 95% bootstrapped confidence
141 intervals.

142 Low dimensional organization of thalamic task-evoked activity

143 We first sought to determine the low-dimensional organization of task-evoked

144 responses in the human thalamus. We used a general linear modeling approach to

145 characterize the task-evoked blood-oxygen-level-dependent (BOLD) activity patterns

146 and estimated the magnitude of BOLD evoked responses for every task ("task betas").

147 Task betas were extracted for every thalamic voxel and every task and compiled into a

148 voxel-by-task activity matrix for each dataset. The cross-subject averaged matrix was

149 subjected to a principal component analysis (PCA) to decompose multi-task evoked

150 activity patterns into a linear summation of a voxel-by-component weight matrix

151 multiplied by a component-by-task loading matrix (Figure 1A). The voxel-by-

152 component weight matrix can be conceptualized as sets of basis patterns of thalamic

153 activity components engaged by different tasks. Similar to previous studies that focused

154 on cortical activity patterns (Nakai and Nishimoto, 2020; Shine et al., 2019a), this

155 analysis revealed a low-dimensional organization, in which the top thalamic activity

156 components can explain up to 60% of the variance across tasks, and each task is

157 associated with a weighted sum of these components (Figure 1B, Figure 1 – Figure

158 Supplements 1-2). Repeating the PCA for each subject (without averaging across

159 subjects) showed that this low-dimensional organization is also observed in individual

160 subjects, where variances across task-evoked activity patterns in the human thalamus

161 can be explained by a low number of components relative to the larger number of

162 cognitive tasks administered (Figure 1C).

163

164

165 Hub organization of thalamic task-evoked activity

166 Examining the spatial patterns of thalamic components (Figure 1B) revealed that several

167 thalamic subregions showed spatial overlap across multiple components, which

168 suggests that these thalamic subregions may flexibly support multiple tasks. We

169   reasoned that if a thalamic voxel is broadly participating in multiple functional domains,

170   it will express a strong weight in components that explained more variances across

171   tasks. Therefore, to further map task-flexible regions in the human thalamus, we

172   calculated a task hub metric by summing each voxel's absolute component weight

173   multiplied by the percentage of variance explained by each component. Results showed

174   that the anterior, medial, medio-posterior, and dorsal thalamus exhibited strong task

175   hub properties (Figure 2A); we had also previously identified these same thalamic

176   subregions as network hubs (Hwang et al., 2017).

177

178   Network hubs in the human thalamus exhibit diverse functional connectivity patterns

179   interlinking multiple cortical systems (Greene et al., 2020; Hwang et al., 2017). To

180   determine whether the tasks hubs we identified correspond to network hub regions

181   previously identified in the thalamus, we compared the spatial similarity of task hubs

182   with functional connectivity hubs (FC hubs). We calculated a network hub metric, the

183   participation coefficient (Gratton et al., 2012; Guimerà and Nunes Amaral, 2005), for

184   every thalamic voxel using timeseries after removing task-evoked variances from the

185   preprocessed fMRI data. The task hubs showed significant spatial correspondence with

186   FC hubs (Figure 2A; spatial correlation: MDTB mean = 0.17, SD = 0.083, $p < 0.001$; N&N

187   mean = 0.17, SD = 0.05, $p < 0.001$). One discrepancy we identified was the posterior

188   thalamus, which showed strong task hub but not network hub property for the MDTB

189   dataset. We then projected the task hubs estimates onto the cortex by calculating the dot

190   product between each thalamic voxel's task hub estimate and its thalamocortical FC

191   matrix. We found that tasks hubs were most strongly coupled with associate regions in

192   the frontal and parietal cortex, for example the lateral frontal, the insula, the dorsal

193   medial prefrontal, and the intraparietal cortices (Figure 2B), regions previously

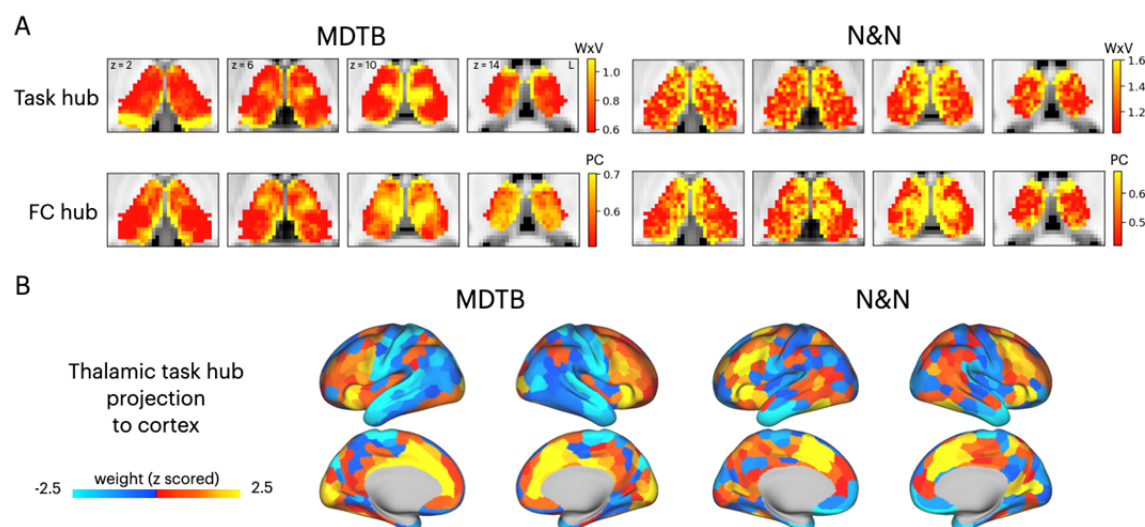194   identified as cortical network hubs (Bertolero et al., 2018, 2015).

Figure 2. Hub regions in the thalamus. (A) Task hubs and FC hubs in the thalamus. WxV = component weight x variances explained by each component. PC = participation coefficient. (B). Projecting task hub metrics onto the cortex via thalamocortical FC.

Thalamocortical interactions transform cognitive task activity

To further test whether thalamic task-evoked activity can support diverse cognitive functions putatively implemented by distributed cortical activity, we adapted the activity flow mapping procedure (Cole et al., 2016; Ito et al., 2017) to assess whether thalamocortical interactions can plausibly transform thalamic task-evoked responses to cortical task activity (Figure 3A). Briefly, for every thalamic voxel, we calculated the dot product between the thalamic evoked response pattern of each task and the thalamocortical FC matrix. This calculation yielded a predicted cortex-wide activity pattern for every task, which can be compared to the observed cortical activity pattern using Pearson correlation. One null model randomly shuffled thalamic evoked responses (the "null model") while the other one set all thalamic evoked responses to a uniform value across all voxels (the "uniformed evoked model"). Both null models assumed no spatial structure in thalamic task-evoked responses, and the uniformed evoked model further assumed that cortical activity patterns are determined only by the summated inputs from thalamocortical FC patterns. We found that across tasks, our thalamocortical activity-flow model outperformed the null models (Figure 3B; MDTB thalamocortical model: mean pattern correlation across tasks = 0.39, SD = 0.1; MDTB

216   null model: mean r = 0.09, SD = 0.053; MDTB uniformed evoked model: mean r = -0.002,

217   SD = 0.11; MDTB thalamocortical model vs null model: t(24) = 15.27, p < 0.001; MDTB

218   thalamocortical model vs uniformed evoked model: t(24) = 14.13, p < 0.001; N&N

219   thalamocortical model: mean pattern correlation across tasks = 0.23, SD = 0.064; N&N

220   null model: mean r = 0.073, SD = 0.044; N&N uniformed evoked model: mean r = -0.021,

221   SD = 0.22; N&N thalamocortical model vs null model: t(102) = 28.4, p < 0.001; N&N

222   thalamocortical model vs uniformed evoked model: t(102) = 17.98, p < 0.001). These

223   results indicate that thalamocortical interactions carry task information.

224

225   We then sought to compare our thalamocortical activity flow model to other cortical

226   and subcortical regions. We constructed a series of comparison models by applying the

227   same activity flow mapping procedure to 100 cortical regions of interests (ROIs) that

228   had similar size as the thalamus (Schaefer et al., 2018), as well as to other subcortical

229   regions including the hippocampus, the caudate, the putamen, and the globus pallidus

230   (Figure 3B). We found that several cortical regions also showed strong prediction

231   performance, including the insula, the inferior frontal cortex, the dorsal medial frontal

232   cortex, the intraparietal sulcus, and the visual cortex (Figure 3C; For a detailed list of

233   prediction results for every ROI and every task, see Figure 3-Supplement File-1).

234   However, the thalamocortical model outperformed all comparison models except

235   cortical ROIs from the visual cortex from the N&N data. These results indicate that

236   thalamocortical interaction is one of the strongest predictors of cortical task activity.
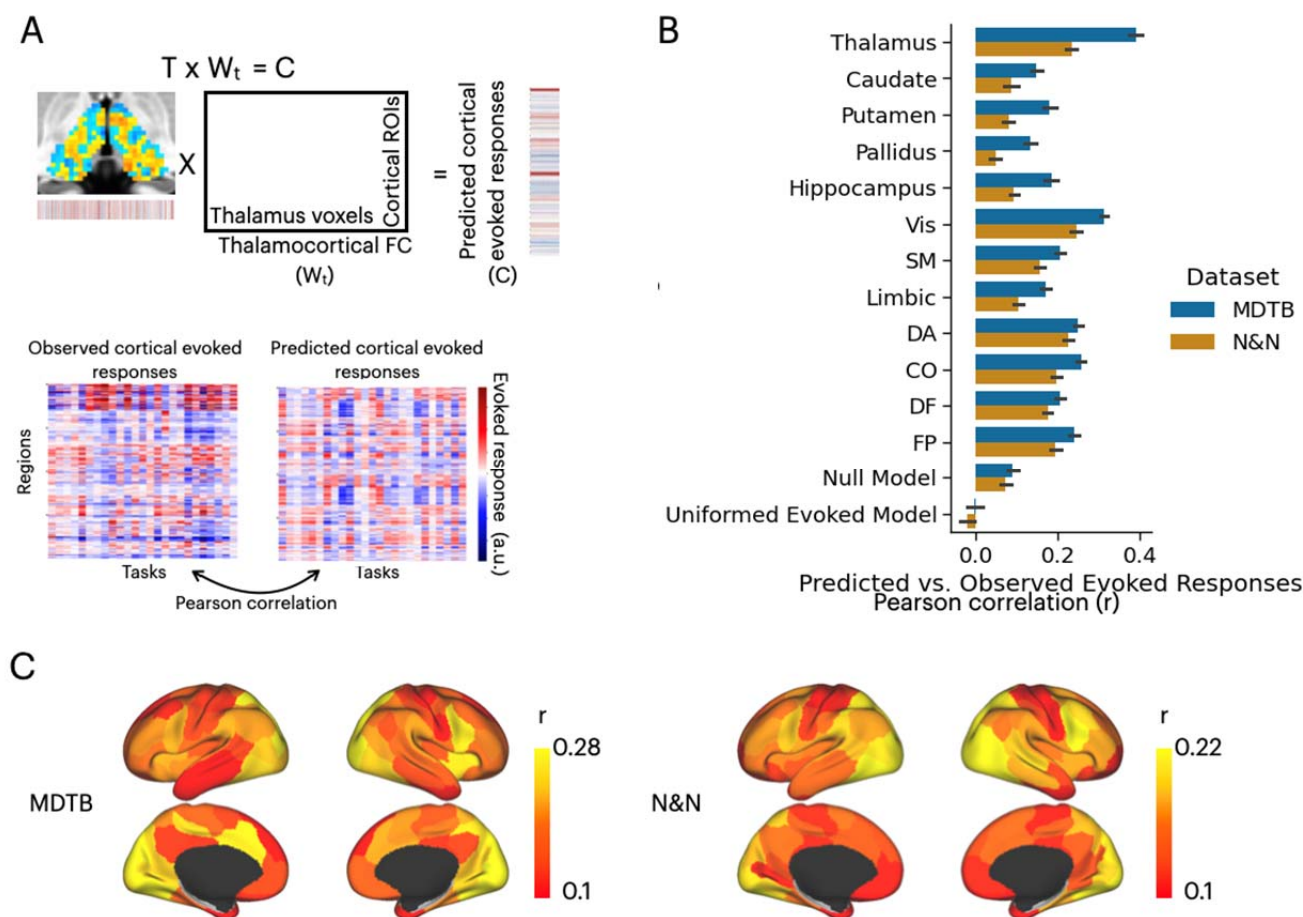
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Figure 3. Thalamus multi-task activity and its influence on multi-task cognitive activity in the cortex. (A) Model for testing whether patterns of cortical task-evoked responses can be predicted by thalamic task-evoked activity transferred through thalamocortical FC. (B) Compared to other brain structures, thalamic task-evoked activity has the strongest predictive power of multi-task cortical activity patterns. Cortical regions divided by 7 cortical functional networks: Vis = visual, SM = somatomotor, DA = dorsal attention, CO = cingulo-opercular, DF = default mode, FP = frontal parietal; for a detailed list of prediction results for every ROI and every task see Figure 3- Supplemental data 1. Null model: randomly permute the evoked pattern in the thalamus. Uniformed model: setting thalamic evoked responses to uniform across all voxels. Error bars indicate 95% bootstrapped confidence intervals. (C) In addition to the thalamus, the visual cortex, the insula, the inferior frontal cortex, the intraparietal sulcus, the medial frontal cortex, and the precentral sulcus also showed strong activity predictions.

Representation geometry predicted from thalamocortical interactions

In addition to predicting activity patterns for individual tasks, we also tested whether

thalamocortical activity-flow can predict the dissimilarity among task activity patterns,

a measure also known as representational geometry (Kriegeskorte and Kievit, 2013).

256 Specifically, representation geometry seeks to capture the topography of task

257 representations by characterizing the multivariate distance among activity patterns for

258 each task. We calculated the representational dissimilarity matrix (RDM) using

259 Spearman correlation from both the predicted and observed cortical activity patterns

260 (Figure 4A). Predicted and observed RDMs were then compared using Kandal's Tau

261 (Nili et al., 2014). We found that across subjects, the thalamocortical activity-flow model

262 performed significantly better than the two null models (MDTB thalamocortical model:

263 mean tau = 0.34, SD = 0.11; MDTB null model: mean r = 0.17, SD = 0.077; MDTB

264 uniformed evoked model: mean r = 0.012, SD = 0.037; MDTB thalamocortical model vs

265 null model: t(20) = 8.35, p < 0.001; MDTB thalamocortical model vs uniformed evoked

266 model: t(20) = 13.82, p < 0.001; N&N thalamocortical model: mean tau = 0.18, SD = 0.064;

267 N&N null model: mean r = 0.12, SD = 0.054, N&N uniformed evoked model: mean r = -

268 0.0047, SD = 0.27; N&N thalamocortical model vs null model: t(5) = 7.02, p < 0.001;

269 N&N thalamocortical model vs uniformed evoked model: t(5) = 5.84, p = 0.002), and

270 outperformed most comparison models except the visual cortex and cortical regions in

271 the DA network for the N&N dataset (Figure 4B; For a detailed list of prediction results

272 from all ROIs and tasks see Figure 4-Supplementary File-1). We note that the predicted

273 RDM suggests the thalamocortical activity flow model showed differences in activity

274 patterns between tasks, as the predicted distances varied. In addition to the thalamus,

275 comparison models constructed with activity patterns from the insula, the dorsal

276 medial prefrontal cortex, the precentral sulcus, the inferior frontal cortex, the

277 intraparietal sulcus, and the visual cortex also showed strong prediction of

278 representational geometry, but weaker than the thalamus (Figure 4B-C). These results

279 indicate that thalamocortical interaction provides one of the strongest contributions to

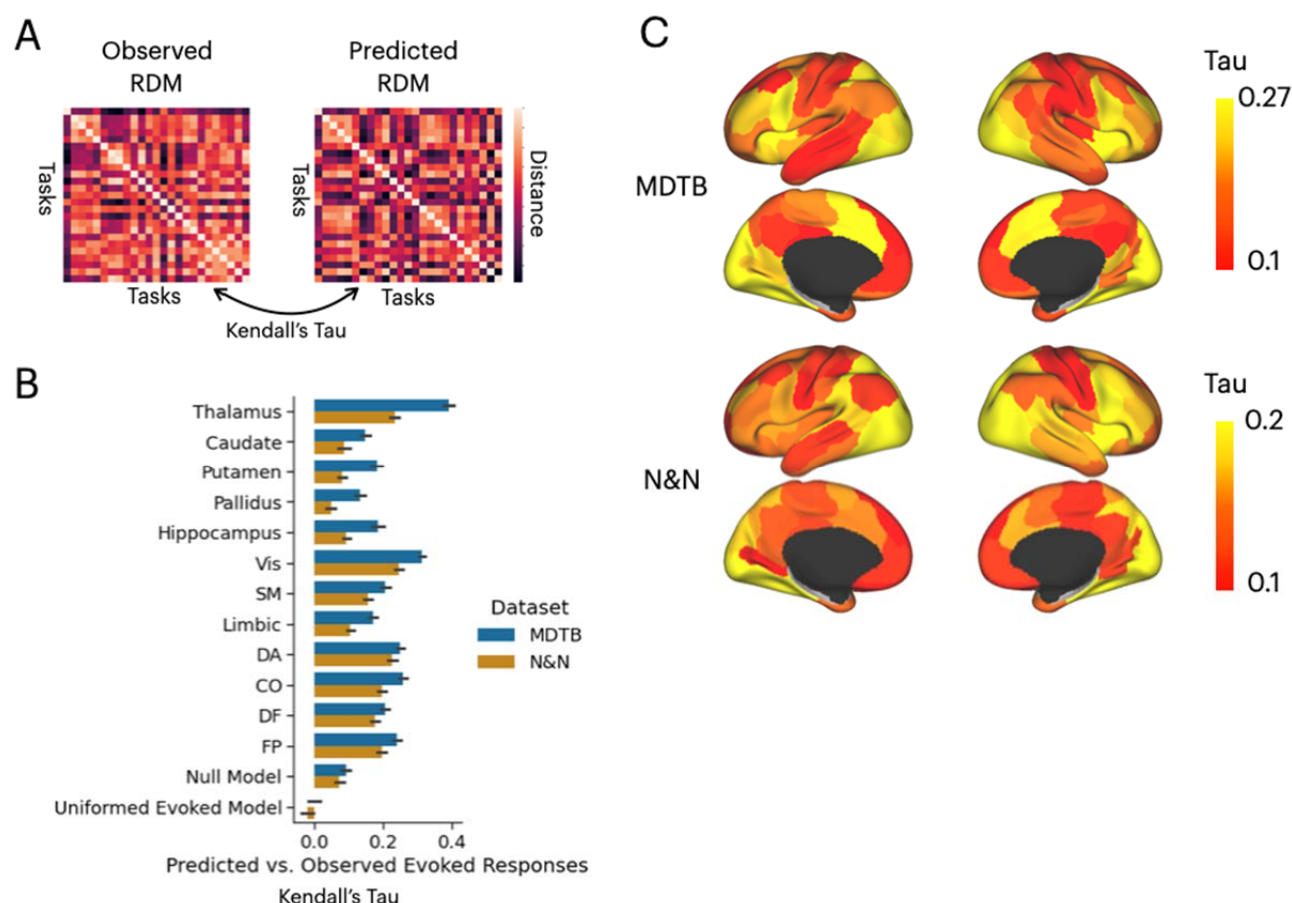280 cortical representational geometry across multiple functional domains.

Figure 4. Thalamus multi-task activity and its influence on multi-task representational geometry in the cortex (A) Model for testing whether multi-task representational geometry constructed from observed cortical responses can be predicted by thalamocortical activity flow (Figure 3) (B) Compared to other brain structures, thalamic task-evoked activity showed stronger predictive power of multi-task representational geometry than most comparison models. Cortical regions divided by 7 cortical functional networks: Vis = visual, SM = somatomotor, DA = dorsal attention, CO = cingulo-opercular, DF = default mode, FP = frontal parietal. For a detailed list of prediction results for every ROI and every task see Figure 4- Supplemental data 1. Null model: randomly permute the evoked pattern in the thalamus. Uniformed model: setting thalamic evoked responses to uniform across all voxels. Error bars indicate 95% bootstrapped confidence intervals. (C) In addition to the thalamus, the visual cortex, the insula, the inferior frontal cortex, the medial frontal cortex, the intraparietal sulcus, and the precentral sulcus also showed strong predictions.

Lesions to task hubs in the thalamus are associated with impaired prediction of task reorientations and representational geometry

The results presented in figures 3 and 4 demonstrated that thalamic task-evoked responses can be transformed to cortical activity patterns to putatively support

300   cognitive representations via thalamocortical interactions. However, it is unclear to

301   what degree task hubs in the thalamus (Figure 3A) contribute to these results. One

302   possibility is that all thalamic voxels contribute equally to cortical task activity patterns.

303   Another possibility is that, since thalamic task hubs are broadly engaged by multiple

304   tasks and exhibited diverging connectivity patterns with multiple cortical systems,

305   thalamic task hubs have a stronger contribution to predicting cortical task activity

306   patterns. To evaluate this prediction, we performed virtual lesion simulations.

307   Specifically, we systematically removed 20% of thalamic voxels based on their

308   percentile rank of task hub estimates and calculated the percentage of reduction in

309   prediction accuracy from the activity-flow analysis. For both datasets, we found that

310   removing voxels with strong task hub estimates decreased the prediction accuracy in

311   cortical task-evoked activity patterns (Figure 5A) and representational geometry (Figure

312   5C). We fitted a regression model to test the relationship between reduction in

313   prediction and percentile rank of task hub metrics removed, and found significant

314   negative associations (MDTB activity flow prediction: $b = -0.43$, $SE = 0.019$, $t = -22.63$, p

315   < 0.001; N&N activity flow prediction: $b = -0.1$, $SE = 0.028$, $t = -3.79$, $p < 0.001$; MDTB

316   RDM prediction: $b = -0.61$, $SE = 0.029$, $t = -21.3$, $p < 0.001$; N&N RDM prediction: $b = -$

317   0.6454, $SE = 0.066$, $t = -9.72$, $p < 0.001$). These results indicate that virtual lesioning of

318   thalamic task hubs had a stronger impact on reducing the model's ability to predict

319   cortical activity patterns. Furthermore, thalamic voxels with the strongest impact on

320   prediction performance were spatially located in the anterior, medial, mediodorsal, and

321   medial posterior thalamus that we previously identified as task hubs (Figure 5B and

322   Figure 5D).

323

324   We compared these simulation results with neuropsychological impairments found in

325   20 human patients with focal thalamic lesions. Neuropsychological profiles of these

326   patients were described in detail in our previous publication (Hwang et al., 2021).

327   Briefly, patients performed a battery of neuropsychological tests to assess executive,

328   language, memory, learning, visuospatial, and construction functions (Lezak et al.,

329   2012). Test performance was then compared to published, standardized norms and

330   converted to z-scores quantify the severity of impairment (Figure 6A). Patients were

331   grouped into two groups, those that showed impairment (z-score < -1.695, worse than

332   95 percentile of the normative population) in single or fewer domains (the SM group)

333   versus those showed impairment across multiple domains (the MM group; Figure 6B).

334   There were no statistically significant differences in the lesion volumes between these

335   two groups of patients (MM group: mean = 1559 mm^3, SD = 1370 mm^3; SM group: mean

336   = 1073 mm^3, SD = 925 mm^3; group difference in lesion size, $t(18) = 0.87$ $p = 0.39$).

337

338   Lesion sites from each group were compared to the effects of the simulated lesions

339   presented in Figure 6B-D. Specifically, we compared the percentages of reduction in

340   voxels from these two groups of lesions. We found that simulated lesions to voxels that

341   overlapped with lesion sites in the MM patient group showed larger reductions in task

342   activity predictions for the N&N dataset but not the MDTB dataset (Figure 6C; MDTB:

343   Komogorov-Smirnov Test D = 0.048, p = 0.065; N&N: Komogorov-Smirnov Test D =

344   0.25, p < 0.001). Parallel findings were also observed for representational geometry

345   (Figures 6D; MDTB: Komogorov-Smirnov Test D = 0.17, p < 0.001; N&N: Komogorov-

346   Smirnov Test D = 0.28, p < 0.001). These empirical results from human patients support

347   our simulated lesion analyses, suggesting that lesioning task hubs in the human

348   thalamus are associated with behavioral deficits across functional domains.
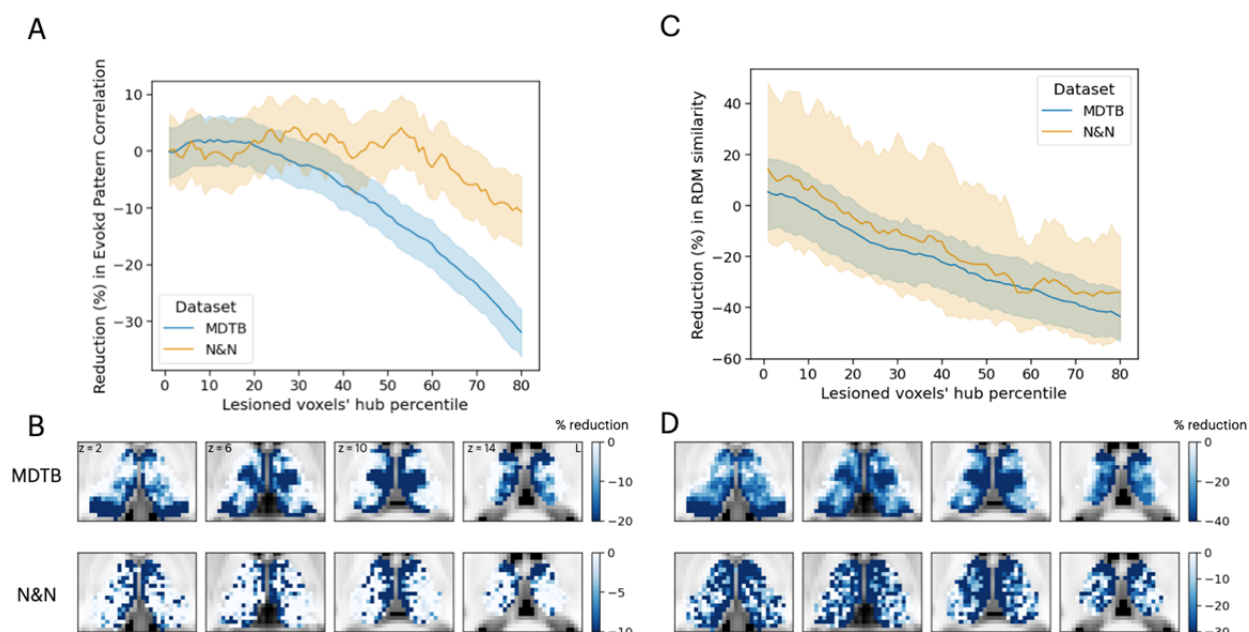
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Figure 5. Simulating the thalamic lesion's effect on multi-task evoked pattern similarity and representational geometry. (A) Artificial lesion of 20% of the thalamus voxels based on their percentile rank of task hub property: examination of the impact on task activity prediction. (B) Subregions that showed greater reduction in prediction accuracy were primarily located in anterior, medial, and posterior thalamus. (C) Artificial lesion of 20% of the thalamus voxels based on their percentile rank of task hub property: examination of the impact on representation geometry prediction. (D) Subregions that showed greater reduction in prediction accuracy of representation geometry showed spatial correspondence with task hubs in the thalamus. Shaded error indicates 95% bootstrapped confidence intervals.
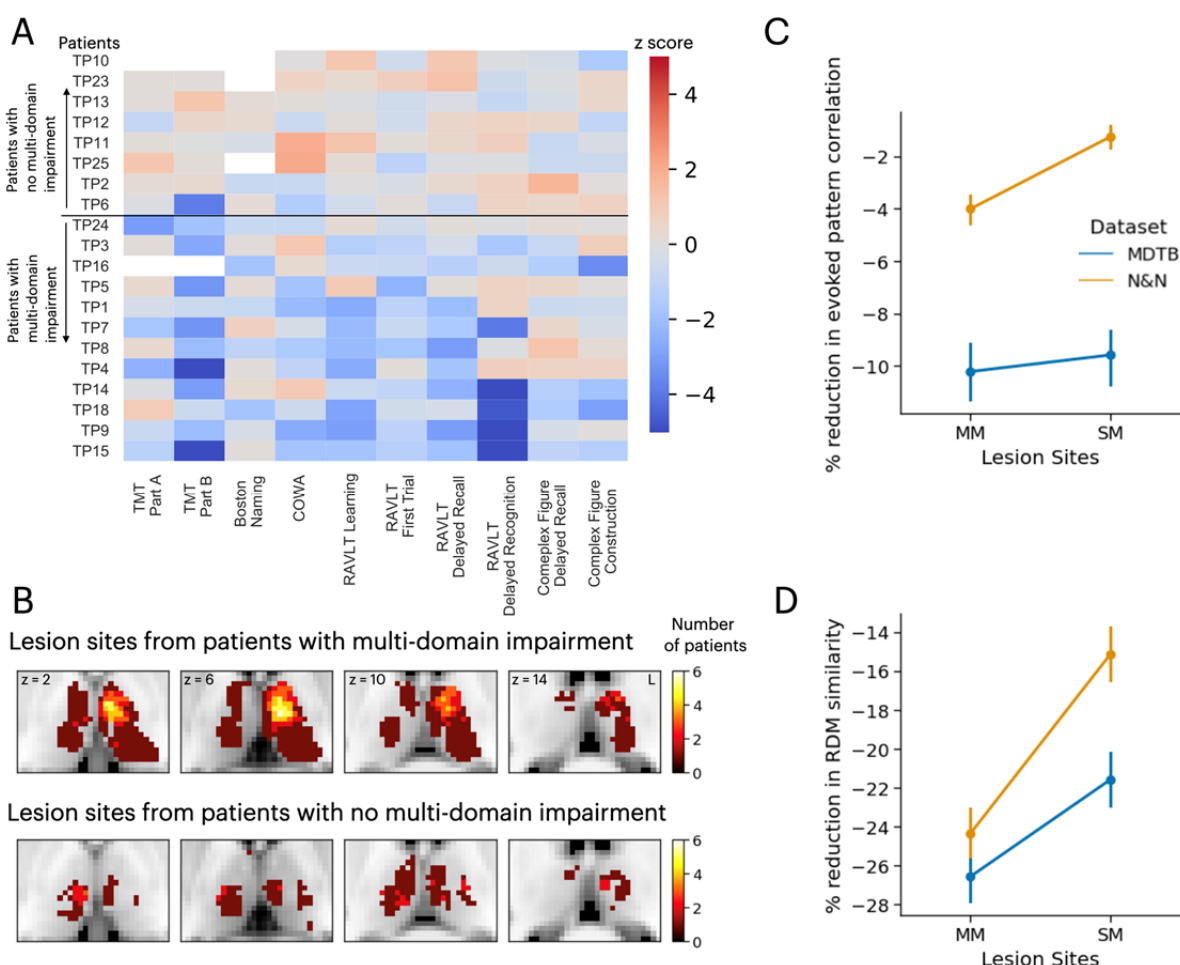
Figure 6. Neuropsychological evaluations from 20 patients with focal thalamic lesions. (A) Twelve patients exhibited multi-domain (MM) impairment (negative z-scores) across multiple neuropsychological assessments. Eight patients exhibited no multi-domain (SM) impairment. (B) Lesion sites from patients with and without multi-domain impairment. (C-D) Mean and 95% bootstrapped confidence interval of the reduction activity prediction after virtual lesions, plotted separately for virtual lesion sites that overlapped with MM or SM lesions. Lesion sites associated with multi-domain impairment also associated with a larger reduction in multi-task pattern similarity after simulated lesions (C) and in representational geometry (D). Figure 6A reproduced from Hwang et al., 2021 with permission.

Discussion

It was hypothesized that the thalamus influences cognitive representations beyond sensory and motor domains (Halassa and Sherman, 2019; Wolff and Vann, 2019). Anatomically, every cortical region receives inputs from one or many thalamic

376   subregions, and most thalamic subregions send signals to one or many cortical systems

377   (Jones, 2001; Sherman, 2007). Functionally, resting-state fMRI studies have found a

378   complete representation of intrinsic cortical networks in the human thalamus (Greene et

379   al., 2020; Hwang et al., 2017; Yuan et al., 2016; Zhang et al., 2008). Several of these

380   networks, such as the FP, CO, and DF, have been implicated in multiple cognitive

381   functions (Sadaghiani et al., 2010; Seeley et al., 2007). These observations raised a

382   broader question of if and how the human thalamus contributes to cognitive task

383   activity across functional domains – the central question we sought to address in this

384   study.

385

386   For the current study, we investigated how thalamic task-evoked activity and

387   thalamocortical functional interactions are organized. We identified several key

388   organizational characteristics pertaining to these activities. First, similar to cortical task

389   activity, thalamic task-evoked activity exhibited a low-dimensional organization, in

390   which a relatively low number of activity patterns can explain a large amount of the

391   variances observed in multi-task thalamic activity patterns. Second, the anterior, medial,

392   and posterior-medial thalamus were more functionally flexible and participated in

393   multiple tasks, and these "task-hubs" spatially overlapped with FC hubs mapped in our

394   previous studies (Hwang et al., 2021, 2017). Third, thalamocortical functional

395   interactions transform thalamic task-evoked activity to task-specific activity patterns in

396   the cortex. Critically, when compared to other brain structures, this thalamocortical

397   activity flow model performed the best in predicting cortical task activity, further

398   highlighting the capacity of the thalamus in influencing distributed activity patterns

399   that may instantiate cognitive representations. Finally, findings from the

400   thalamocortical activity flow model were further corroborated by simulated lesions and

401   neuropsychological impairments observed in patients with focal thalamic lesions,

402   affirming the behavioral significance of thalamocortical interactions. Collectively, these

403   findings highlight a general and critical role of thalamocortical interactions supporting

404   cognitive functions.

405

406 Neural systems support a rich and diverse behavioral repertoire. Findings from both

407 human functional neuroimaging and animal models now point to the low-dimensional

408 structure as a key organizational characteristic that interlinks spatiotemporal neural

409 activity and behavior (Beam et al., 2021; Karolis et al., 2019; MacDowell and Buschman,

410 2020; Nakai and Nishimoto, 2020; Shine et al., 2019a). For example, a large-scale meta-

411 analysis on more than 10,000 neuroimaging studies found that activity patterns across

412 83 behavioral tasks can be summarized by 13 latent components (Yeo et al., 2016). This

413 study formalized the notion that task performance depends on sets of cognitive

414 components, and that the neuroanatomical distribution of task-evoked activity has a

415 low-dimensional organization. Behaviorally, similar observations have also been

416 reported in the clinical profiles from human stroke patients (Bisogno et al., 2021),

417 demonstrating that three components can explain 50% of behavioral deficits across

418 neuropsychological batteries. Analogous findings have also been reported for the

419 temporal dynamics of neural activities, in which spatiotemporal patterns associated

420 with memory, social, emotion, and language tasks correspond to the temporal flow

421 within a low-dimensional state space (Shine et al., 2019a). Altogether, these studies

422 suggest that an elementary set of processes can be deployed adaptively to support

423 processing demands across different tasks.

424

425 However, most prior studies focused on cortical activity patterns, therefore one

426 contribution of our study was to identify a low-dimensional activity structure in the

427 human thalamus. This observation may refine our understanding of thalamic

428 contributions to human cognition. For example, the thalamus itself likely does not

429 encode high-dimensional, vivid, cognitive representations for each individual task.

430 Instead, thalamocortical circuits may support a few key, common but significant,

431 functions across tasks. Notably, the thalamic task components we observed expressed

432 strongest weights in anterior, medial, and posterior thalamus but not in lateral thalamic

433 regions that overlap with first-order thalamic relays such as the lateral geniculate

434   nucleus and the ventrolateral nucleus. This observation suggests that the thalamus

435   likely supports functions beyond basic sensorimotor relay, some of which were

436   suggested by previous studies, and include selection and gain control (Halassa and

437   Kastner, 2017), adjustment of inter-regional communication (Hwang et al., 2020b;

438   Saalmann et al., 2012), and modulation of cortical excitability (Kosciessa et al., 2021).

439   The small size of the thalamus further suggests a prominent role in modulating the low-

440   dimensional organization of task-evoked cortical activity – for instance, previous

441   studies have found that thalamic activity correlates with the dimensionality and the

442   strength of cross-system coupling between cortical regions (Garrett et al., 2018; Shine et

443   al., 2019b). These thalamocortical processes may be required for behavioral performance

444   across many different tasks, driving the low-dimensional organization we observed.

445

446   Our findings further support proposals suggesting that the human thalamus, by virtue

447   of its unique connectivity profile, may be in an ideal position to influence cortex-wide

448   task activity (Garrett et al., 2018). Because every cortical region receives inputs from one

449   or multiple thalamic regions, thalamocortical interactions may be more effective in

450   pushing cortical activity patterns to the desired task state. We speculate that the

451   thalamus may be at the nexus where specific activity patterns in the thalamus can be

452   selectively down- or up-regulated to meet the specific information processing demands

453   of different tasks. This hypothesis predicts that thalamocortical interactions should

454   transfer task-specific information between the thalamus and the cortex, a prediction we

455   tested in our thalamocortical activity flow analysis. Specifically, we constructed an

456   activity flow mapping model to test whether thalamocortical interactions can transfer

457   thalamic task-evoked responses to cortical task activity. We found that our data-driven

458   thalamocortical model can indeed successfully predict task-specific activity patterns

459   and multi-task representational geometry observed in the cortex, better than null

460   models that assumed thalamocortical interactions do not carry task-specific information.

461   Furthermore, past studies that adopted similar activity flow mapping approaches have

462   shown that including all regions across the whole brain can predict task-specific activity

463   patterns with very high accuracy (Cole et al., 2016). Our study tested a different

464   question to evaluate the predictive power of the thalamus relative to other brain regions.

465   Critically, we found that the thalamocortical model outperformed comparison models

466   constructed with other cortical and subcortical structures, including frontal (the insula

467   and the inferior frontal sulcus), parietal, and striatal regions previously implicated in

468   adaptive control of tasks (Badre and Nee, 2018; Ito et al., 2022). These results suggest

469   that thalamocortical interactions likely exert a strong influence on cortical activity that

470   may instantiate cognitive representations.

471

472   Placing the thalamus in a central position for influencing cortex-wide cognitive activity

473   has several benefits. For instance, the thalamus consists of two classes of

474   thalamocortical projection cells, "matrix" and "core" cells, where core cells target

475   specific granular cortical structures, and matrix cells diffusely project to multiple brain

476   regions (Jones, 2001). Given that different brain regions may be encoding different

477   perceptual and cognitive information (Christophel et al., 2017), selectively modulating

478   thalamic activity may facilitate targeted activations of cortical representations via

479   associated thalamocortical interactions. The diffuse projection pattern of matrix cells in

480   the thalamus may simultaneously activate multiple cortical regions and promote inter-

481   system integration when required (Hwang and D'Espostio, 2022; Jones 2001).

482   Furthermore, the thalamus is modulated by inputs from other subcortical structures,

483   such as the reticular nucleus, the basal ganglia, the superior colliculus, and the

484   cerebellum (Bostan and Strick, 2018; Shine, 2020). This anatomical feature suggests that

485   the thalamus may be an efficient target for exerting neuromodulatory (e.g.,

486   dopaminergic) influences on cognitive processes when required (Castro-Alamancos and

487   Gulati, 2014; Garrett et al., 2022). Several computation models have leveraged these

488   characteristics to explain the functions of basal-ganglia-thalamic circuits for higher-

489   order cognitive functions (Jaramillo et al., 2019; O'Reilly and Frank, 2006).

490

491   Another important observation was that the anterior, medial, and posterior thalamus

492   exhibited "task hub" property, that is, are more flexibly recruited by multiple thalamic

493   activity components. These subregions overlapped with thalamic FC hubs that we

494   previously identified (Hwang et al., 2017). In the current study, we found that thalamic

495   task hubs were most strongly coupled with the frontal and parietal associative cortices

496   (Figure 2B). Intriguingly, these frontoparietal regions have been hypothesized to be part

497   of a flexible multiple-demand system (Cole et al., 2013; Duncan, 2010; Ito et al., 2022),

498   and thus, these thalamic subregions may be part of a core system whose functions are

499   required to perform specific computations that are common across many different task

500   contexts. One strong test of the behavioral relevance of these thalamic task hubs is to

501   examine the effects of lesions. If thalamic task hubs are part of a domain-general core,

502   lesioning task hubs should be associated with broad behavioral deficits not confined to

503   a specific behavioral domain. Indeed, we found that simulated lesions to thalamic task

504   hubs impaired prediction accuracy in cortical activity pattern across tasks, and stroke

505   lesions to the anterior-medial thalamus in human patients were associated with

506   behavioral deficits across functional domains (Hwang et al., 2021, 2020a). At this point

507   we are agnostic to the specific function these thalamic task hubs perform. One

508   hypothesis, suggested by findings from rodent models, is that the medial thalamus

509   excites task-relevant and inhibits task-irrelevant cortical activity that encode working

510   memory representations (Mukherjee et al., 2021; Rikhye et al., 2018). Thus, in human

511   subjects, thalamocortical interactions between thalamic task hubs and frontoparietal

512   systems may control task representations that bind sensory, motor, and contextual

513   information that are necessary for adaptive behavior across tasks (Schumacher and

514   Hazeltine, 2016). This is an open question that should be evaluated in future studies.

515

516   On important limitation of our study is that our thalamocortical activity flow model

517   cannot establish the directionality of thalamic activity influencing cortical activity. It is

518   more likely that brain systems instantiate cognitive representations via recurrent

519   interactions among cortical regions and the thalamus, as well as integrating inputs from

520   other brain structures. As discussed above, including all brain regions into the activity

521   flow model can substantially improve model performance in predicting task-specific

522   activity patterns (Cole et al., 2016). Nevertheless, our findings suggest that, across the

523   whole brain, the thalamus likely has one of the strongest contributions to cortical task

524   activity. Another important limitation is that the posterior thalamus exhibited strong

525   task hub property in the MDTB dataset but not the N&N dataset. We suspect this could

526   be related to differences in behavioral tasks across the two datasets, and speculatively,

527   to the increased noise in the N&N dataset, given the lower number of observations per

528   task and lower subcortical signal-to-noise ratio. One strong test of mapping task hubs is

529   the lesion methods, and in our previous study (Hwang et al., 2021) we did not have

530   good lesion coverage on the pulvinar nucleus. Future studies should test whether

531   patients with pulvinar lesions have cognitive deficits beyond visual attention tasks

532   (Snow et al., 2009).

533

534   To conclude, our study reported two important organizational principles of how

535   thalamic task-evoked activity and thalamocortical interactions support cognitive tasks.

536   Thalamic task-evoked activity has a low-dimensional structure, and thalamocortical

537   interactions have a strong influence on generating task-specific cortical activity patterns.

538   These results highlight how the thalamus is in a central position for supporting

539   cognitive task representations.

540

541   **Methods**

542

543   <u>Datasets</u>

544   We analyzed two datasets, the multi-domain task battery dataset (MDTB dataset [King

545   et al., 2019] at https://openneuro.org/datasets/ds002105/) and the Nakai and

546   Nishimoto dataset (N&N dataset [Nakai and Nishimoto, 2020] at

547   https://openneuro.org/datasets/ds002306/). We selected these datasets because both

548   include fMRI data from subjects that performed a large number of tasks across

549   functional domains (Figure 1A). The MDTB dataset included fMRI data from 21 subjects

550   (13 women, 8 men; mean age = 23.28 years, SD = 2.13; we excluded 3 out of the original

551   24 subjects that did not have all tasks available after removing high noise datapoints).

552   MRI Data were collected on a 3T Siemens Prisma with the following parameters:

553   repetition time (TR) = 1 s; 48 slices with 3 mm thickness; in-plane resolution 2.5 × 2.5

554   mm^2; multi-band acceleration factor = 3; in-plane acceleration factor =2; echo time and

555   flip angle were not reported in the original paper. Structural T1 images were acquired

556   using magnetization-prepared rapid acquisition gradient echo sequence (MPRAGE;

557   field-of-view = 15.6 × 24 × 24 cm^3, at 1 × 1 × 1 mm^3 voxel size). The N&N dataset

558   included fMRI data from 6 subjects (2 females, 4 males, age range 22-33 years) collected

559   on a 3T Siemens Tim Trio system. Functional MRI data were collected with the

560   following parameters: TR = 2 s; 72 slices with 2mm slice thickness; in-plane resolution =

561   2 x 2 mm2; echo time = 30 ms; flip angle = 62 degrees; multiband factor = 3. Structural

562   MRI data were collected with a MPRAGE sequence (TR = 2530 ms; TE = 3.26 ms; flip

563   angle=9 degrees; FOV=256 × 256 mm^2; voxel size=1×1×1mm^3).

564

565   <u>MRI data preprocessing</u>

566   Both datasets were preprocessed using fMRIPrep version 20.1.1 (Esteban et al., 2019) to

567   reduce noise and transform data from subject native space to the ICBM 152 Nonlinear

568   Asymmetrical template version 2009c for group analysis (Fonov et al., 2011).

569   Preprocessing steps include bias field correction, skull-striping, co-registration between

570   functional and structural images, tissue segmentation, motion correction, and spatial

571   normalization to the standard space. As part of preprocessing, we obtained nuisance

572   regressors including rigid-body motion estimates, cerebral spinal fluid (CSF), and white

573   matter (WM) noise components from the component-based noise correction procedure

574   (Behzadi et al., 2007). These nuisance regressors were entered in the regression model to

575   reduce the influences from noise and artifacts (see below). We did not perform any

576   spatial smoothing.

577

578   Task-evoked responses

579   The MDTB dataset contained 24 cognitive tasks and a resting condition collected across

580   four scanning sessions; each session consisted of 8 runs. Each task started with a 5

581   second instruction and was followed by 30 seconds of continuous task performance.

582   The N&N dataset contained 103 tasks collected across 18 MRI scanning runs in 3 days.

583   Each task trial lasted 6 to 12 seconds where task instruction was on screen throughout

584   the trial, and each task repeated 12 times distributed across runs. For a complete list of

585   behavioral tasks, see Figure 1A and Figure 1-Supplementary File 1. The detailed design

586   of each task for both datasets were reported in King et al., 2019, and in Nankai &

587   Nishimoto, 2020.

588

589   We employed a voxel-wise general linear modeling (GLM) approach to estimate task-

590   evoked responses, using AFNI's 3dDeconvolve (Cox, 1996). For every voxel, a

591   generalized least squares regression model was constructed and fitted to the

592   preprocessed timeseries with the following regressors: task regressors, rigid body

593   motion regressors and their derivatives, and the top 5 CSF and WM noise components.

594   High motion volumes (framewise displacement > 0.2 mm) were removed from data

595   analyses via the censoring option, and subjects with tasks with more than 40% of the

596   data censored were dropped from further analyses (3 MDTB subjects dropped). For

597   each subject, all imaging runs were concatenated, and signal drifts were modeled

598   separately for each run, including run-specific constant and polynomial regressors. All

599   task regressors were created by convolving a gamma hemodynamic response function

600   with the stimulus duration. The stimulus duration was determined by the specific block

601   or trial design sequence of each task (See Figure 1-Supplementary File 1 for the specific

602   duration used for all tasks). For the MDTB dataset, several tasks contained different

603   sub-conditions, and the GLM estimates of sub-conditions were averaged to obtain one

604   estimate per task. Repeating our analyses without averaging sub-conditions did not

605   change our results. For the MDTB dataset, the 5 s instruction period at the start of each

606   task block was modeled but not included into subsequent analyses. For the N&N

607   dataset, the task instruction was presented simultaneously during all trials, and as a

608   result it could not be separated from the GLM analyses.

609

610   <u>Low-dimensional organization of task-evoked activity in the thalamus</u>

611   To probe the low-dimensional organization of task-evoked activity in the thalamus, we

612   first applied a thalamus mask from the Harvard-Oxford subcortical atlas, which mask

613   was used to extract task-specific evoked response estimates from 2445 thalamus voxels.

614   These estimates were then compiled into a task-by-voxel evoked activity matrix for each

615   subject. This evoked activity matrix was then z-scored by subtracting the grand mean

616   from the whole matrix and divided by the standard deviation across all elements. A

617   principal component analysis decomposed the evoked activity matrix into a linear

618   summation of a voxel-by-component weight matrix multiplied by a component-by-task

619   loading matrix (Figure 1A). The voxel-by-component weight matrix can be

620   conceptualized as sets of basis patterns of thalamic activity components engaged by

621   different tasks. The loading matrix described the relationship between each voxel-wise

622   component map and tasks. We then summated the percentage of variances explained to

623   determine how many components were required to explain more than 50% of the

624   variance observed in the evoked activity matrix. We performed the PCA analysis with

625   and without averaging the evoked activity matrix across subjects. We averaged the

626   matrix before PCA to visualize the voxel patterns of each component and repeated the

627   PCA analysis without averaging separately for each subject to test whether the low-

628   dimensional structure can be replicated at the level of individual subjects.

629

630   <u>Thalamic task hubs</u>

631   Some thalamic subregions could participate in multiple tasks across functional domains,

632   exhibiting "task hub" properties. To map these task hub regions, for every voxel we

633   calculated a WxV metric:

634   $$WxV = \sum_{i=1}^{n} |W_i| \times V_i$$

635 Where $|W_i|$ is the absolute value of weight for component i, V_i is the percentage of

636 variance explained for component i, and n is the number of components. We reasoned

637 that a task hub region would be more strongly recruited by components that explained

638 a large amount of the variances in the evoked activity matrix, exhibiting a higher WxV

639 estimate.

640

641 To compare the task hubs to the FC hubs that we had mapped previously (Hwang et al.,

642 2017), we first obtained a thalamocortical FC matrix using principle component linear

643 regression (Ito et al., 2017) to estimate patterns of FC between each thalamic voxel and

644 400 cortical ROIs (Schaefer et al., 2018). We estimated this FC matrix using residuals

645 after task regression. Note that one advantage of principle component linear regression

646 is that its estimates are similar to partial correlation, accounting for shared variances

647 among signals. We then calculated a connector hub metric participation coefficient for

648 each voxel (Gratton et al., 2012):

649   $PC = 1 - \sum_{s=1}^{N} \left(\frac{K_{is}}{K_i}\right)^2$

650 where K_i is the sum of total FC weight for voxel i, K_{is} is the sum of functional

651 connectivity weight between voxel i and the cortical network s, and N is the total

652 number of networks. To perform this calculation, we assigned the 400 cortical ROIs to

653 seven cortical functional networks, i.e., to the FP, DF, CO, DA, limbic, SM, and visual

654 networks (Schaefer et al., 2018; Yeo et al., 2011). We calculated participation coefficient

655 values across a range of density thresholds of the thalamocortical FC matrix (density =

656 0.01–0.15) and averaged across thresholds.

657

658 To determine which cortical regions showed the strongest coupling with thalamic task

659 hubs, we calculated the dot product between WxV and thalamocortical FC matrix,

660 yielding a project task hub matrix on the cortical space:

661   Cortical $WxV = WxV \cdot FC_{ThxCtx}$

662 where WxV is the 2445 voxel-wise task hub metrics, and FC_{ThxCtx} is the 2445 x 400

663 thalamocortical FC matrix.

664

665 <u>Thalamocortical activity flow mapping</u>

666 To determine whether thalamocortical interactions can transform thalamic task-evoked

667 activity to cortical task activity, we modified the activity flow mapping procedure (Cole

668 et al., 2016; Ito et al., 2017), and for each task and each subject we calculated:

669 $$A_{ctx} = W_t \cdot FC_{ThxCtx}$$

670 where W_t is the evoked response estimate for every thalamic voxel, FC_{ThxCtx} is the

671 thalamocortical FC matrix, and A_{ctx} is the predicted cortical activity pattern. We

672 repeated this analysis for every task, and the predicted cortex-wide activity patterns

673 were then empirically compared to the observed activity patterns using Pearson

674 correlation. In addition to comparing individual task activity patterns, we also

675 compared the predicted versus observed representational geometry. Representation

676 geometry seeks to capture the topography of task representations by characterizing the

677 multivariate distance of activity patterns among tasks. We calculated the

678 representational dissimilarity matrix using Spearman correlation. Predicted and

679 observed representational dissimilarity matrices were compared using Kandal's Tau

680 (Nili et al., 2014).

681

682 To evaluate our thalamocortical activity flow mapping procedure, we compared its

683 results to two different null models and to comparison models. The first null model

684 randomly shuffled the voxel order in W_t, which assumed no task-specific information in

685 thalamic evoked activity pattern. The second null model set W_t to a uniform vector,

686 which assumed that A_{ctx} was entirely determined by the pattern in FC_{ThxCtx}. We

687 constructed a series of comparison models by repeating the same analysis on other

688 source ROIs, including the hippocampus, the caudate, the putamen, and the pallidus,

689 and 100 cortical ROIs (Schaefer et al., 2018) that were similar in size to the thalamus. For

690 these comparison models, we replaced W_t with voxel-wise evoked responses from other

691   source ROIs, and recalculated the FC matrix by calculating FC between every voxel in

692   the source ROI and 400 cortical ROIs using PCA linear regression.

693

694   <u>Lesion analyses</u>

695   We performed additional simulated and empirical lesion analyses to test which

696   thalamic subregions contribute to predicting cortical task activity. For simulated lesions,

697   we ranked thalamic voxels by their task hub (WxV) metrics, then set the evoked

698   responses in 20% of thalamic voxels to zero and repeated the thalamocortical activity

699   flow analysis. We repeated this virtual lesioning procedure for voxels ranking from 0%

700   to 80% in steps of 1%, window size of 20%, and calculated the effects of virtual lesioning

701   of thalamic voxels on predicting both individual task activity pattern and

702   representational geometry. The percentage of prediction reduction (relative to the

703   original observed value) after virtual lesioning was assigned to each voxel to construct

704   voxel-wise maps that depict the effects of simulated lesions.

705

706   We then compared the effects of simulated lesions to lesions observed in human

707   patients with focal thalamic lesions. Details of these patients were reported in our

708   previous study (Hwang et al., 2021). Briefly, these patients were selected from the Iowa

709   Neurological Patient Registry, and had focal lesions caused by ischemic or hemorrhagic

710   strokes restricted to the thalamus (age = 18-70 years, mean = 55.8 years, SD = 13.94

711   years, 13 males). The lesion sites of these patients were manually traced and normalized

712   to the MNI-152 template using a high-deformation, non-linear, enantiomorphic,

713   registration procedure that we described in detail in our previous papers (Hwang et al.,

714   2021, 2020a).

715

716   We further tested whether voxels associated with stronger virtual lesioning effects

717   overlapped with lesion sites associated with more pronounced behavioral deficits in

718   human stroke patients. Behavioral deficits were assessed using a set of standardized

719   neuropsychological tests: (1) executive function using the Trail Making Test Part B

720   (TMT Part B); (2) verbal naming using the Boston Naming Test (BNT); (3) verbal fluency

721   using the Controlled Oral Word Association Test (COWA); (4) immediate learning

722   using the first trial test score from the Rey Auditory-Verbal Learning Test (RAVLT); (5)

723   total learning by summing scores from RAVLT, trials one through five; (6) long-term

724   memory recall using the RAVLT 30-minute delayed recall score; (7) long-term memory

725   recognition using the RAVLT 30-minute delayed recognition score; (8) visuospatial

726   memory using the Rey Complex Figure delayed recall score; (9) psychomotor function

727   using the Trail Making Test Part A (TMT Part A); and (10) construction using the Rey

728   Complex Figure copy test. To account for age-related effects, all test scores were

729   converted to age-adjusted z-scores using the mean and standard deviation from

730   published population normative data. We determined the functional domain that each

731   test assessed, described in Neuropsychological Assessment (Lezak et al., 2012). Twelve

732   out of 20 patients had significant impairment ($z < -1.645$) reported in more than two

733   functional domains, and thus were classified as the multiple-domain (MM) patient

734   group. The rest of the 8 patients had significant impairment in one or fewer domains,

735   and classified as the single-domain (SM) group. We predicted that lesion sites in the

736   MM group would show stronger virtual lesioning effects, when compared to lesion

737   sites in the SM group.

738

739   Code and data availability statement

740   Code and data are available at https://github.com/HwangLabNeuroCogDynamics/

741   ThalamicTaskHubs

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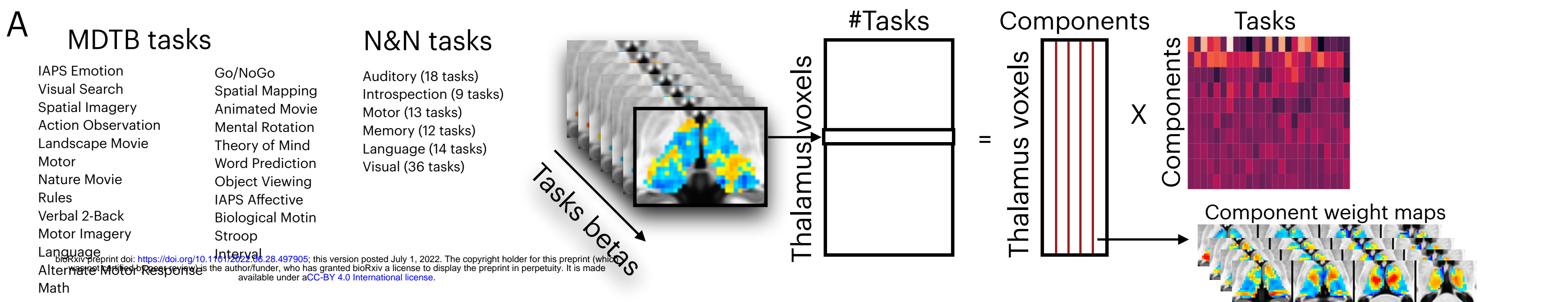816   Modulates Task-Evoked Functional Connectivity. *Cereb Cortex* **30**:875–887.

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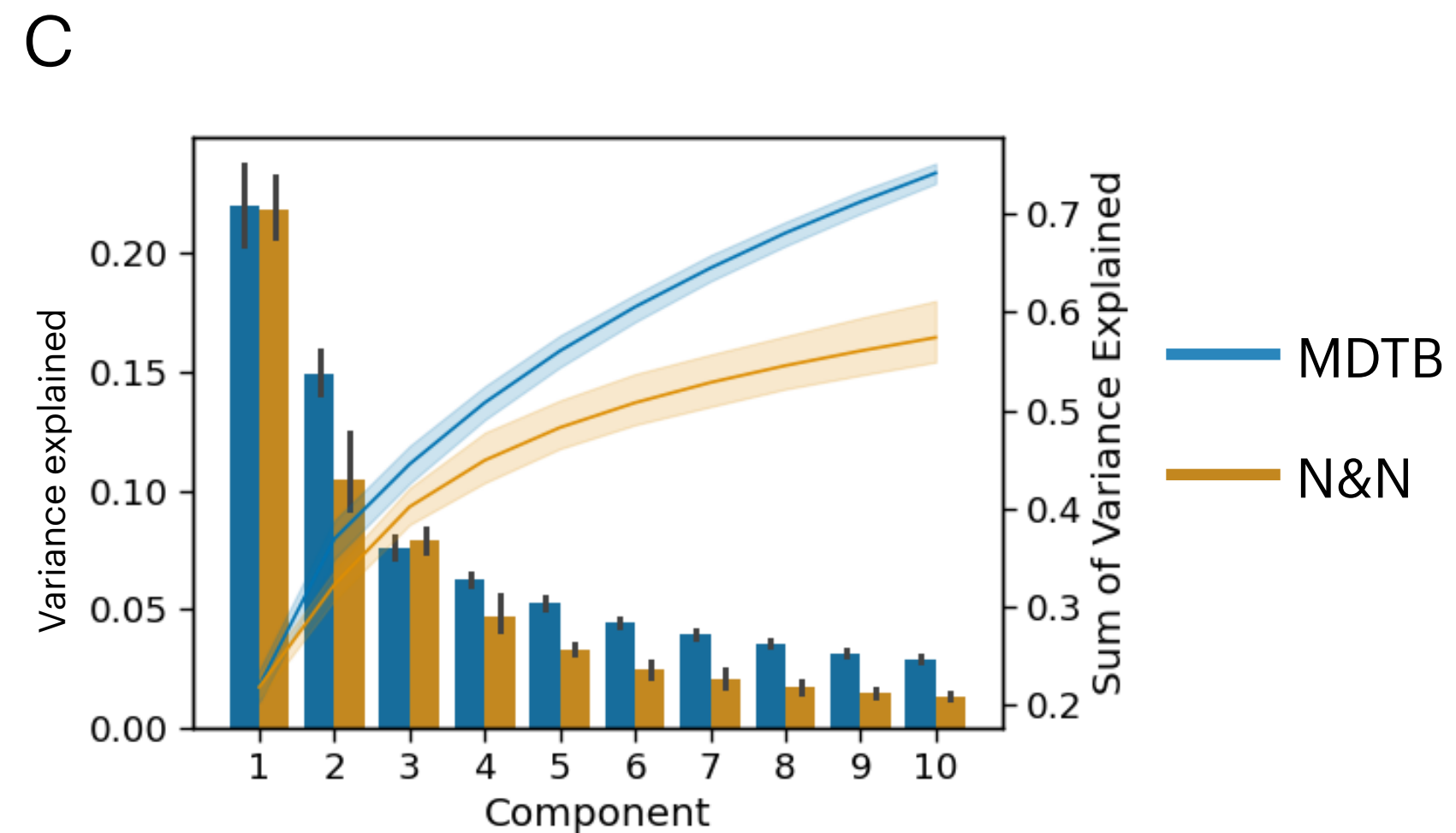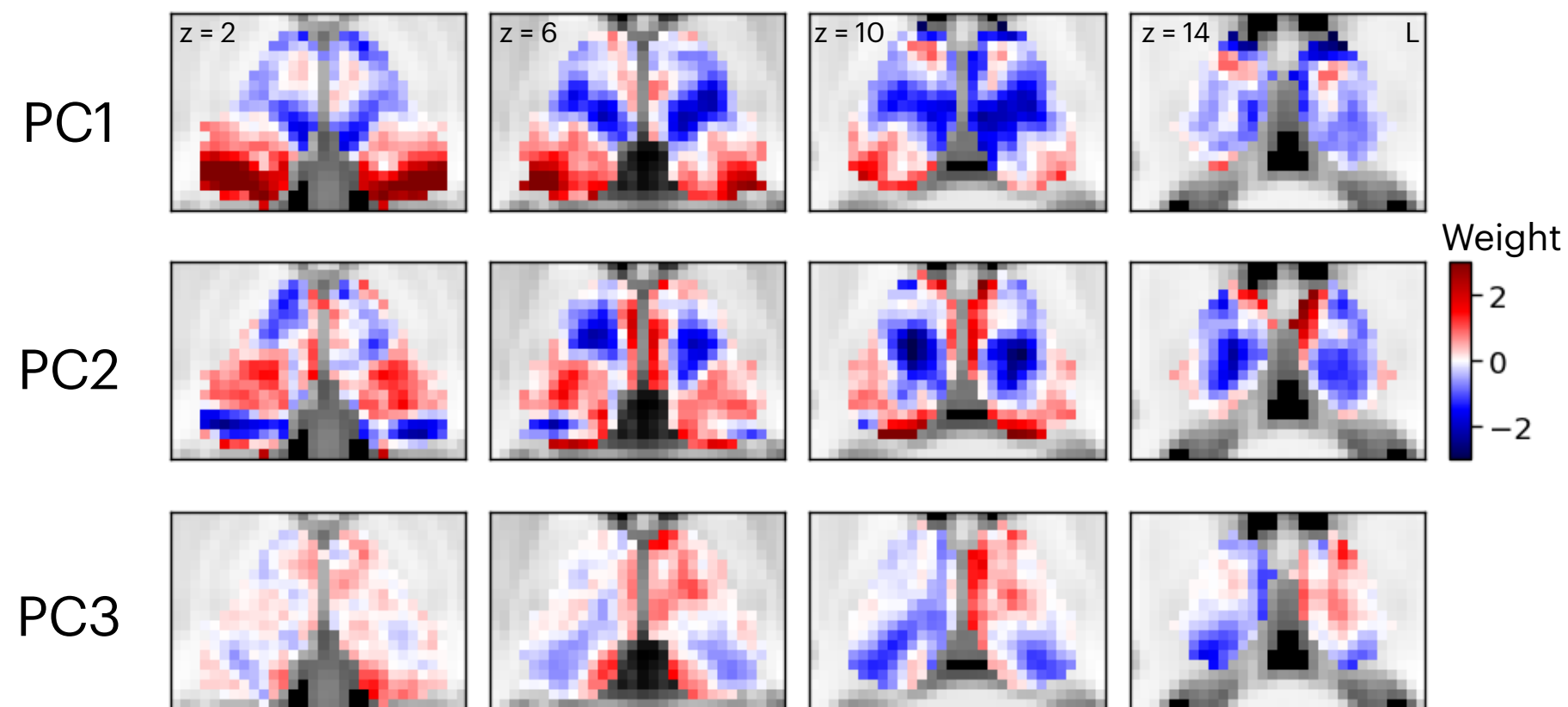
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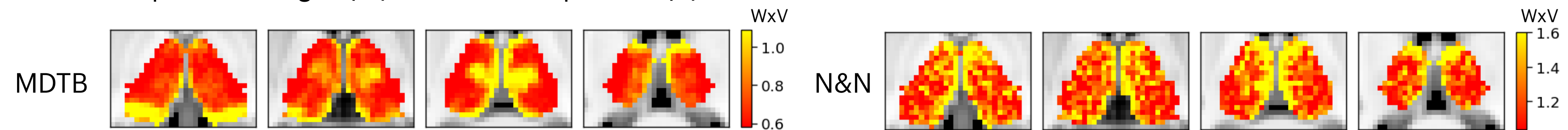867   Response Selection. *Curr Dir Psychol Sci* **25**:449–454.

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A MDTB tasks

IAPS Emotion   Go/NoGo
Visual Search   Spatial Mapping
Spatial Imagery   Animated Movie
Action Observation   Mental Rotation
Landscape Movie   Theory of Mind
Motor   Word Prediction
Nature Movie   Object Viewing
Rules   IAPS Affective
Verbal 2-Back   Biological Motin
Motor Imagery   Stroop
Language   Interval
Alternate Motor Response
Math

N&N tasks

Auditory (18 tasks)
Introspection (9 tasks)
Motor (13 tasks)
Memory (12 tasks)
Language (14 tasks)
Visual (36 tasks)

#Tasks   Components   Tasks

Thalamus voxels = Thalamus voxels X Components

Component weight maps

B Top 3 components that explained ~50% of task variance

PC1   PC2   PC3

Weight

C

D Component Weight (W) * Variance explained (V)
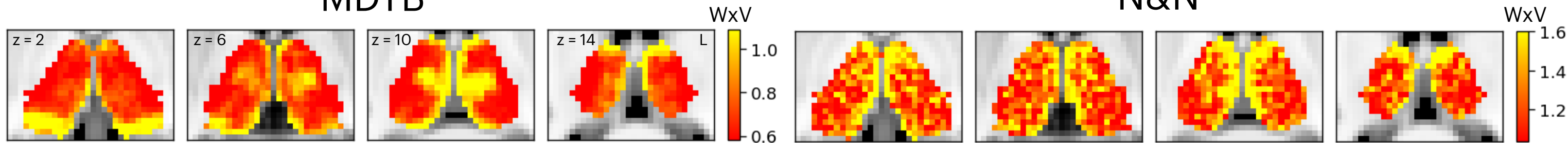
MDTB   WxV   N&N   WxV

A

MDTB   N&N

Task hub

FC hub
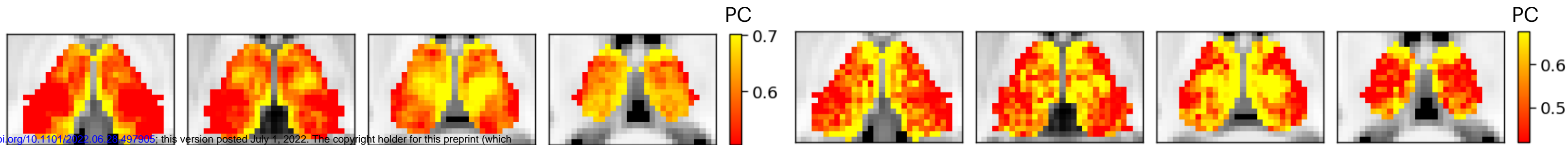
B

MDTB   N&N

Thalamic task hub
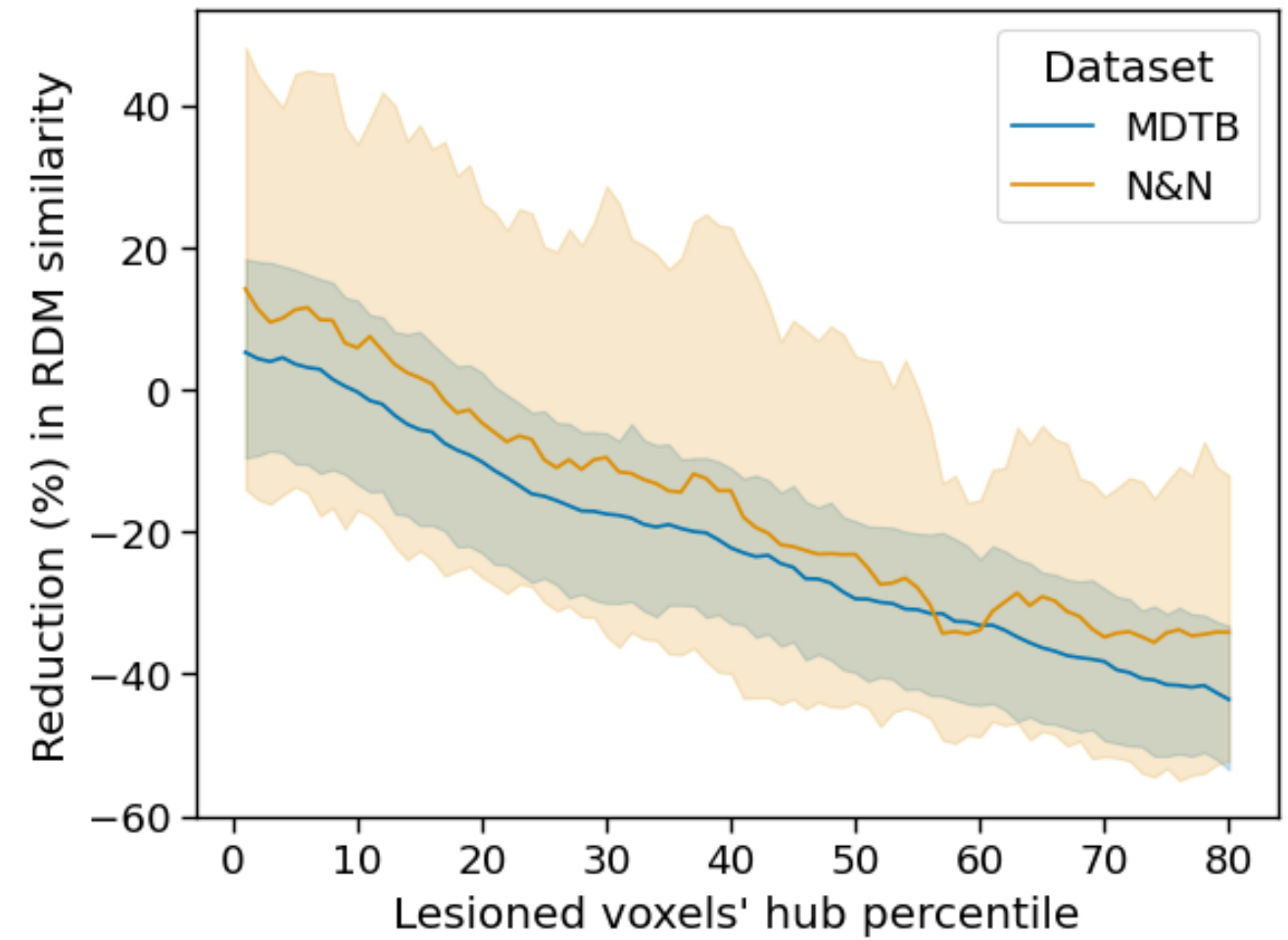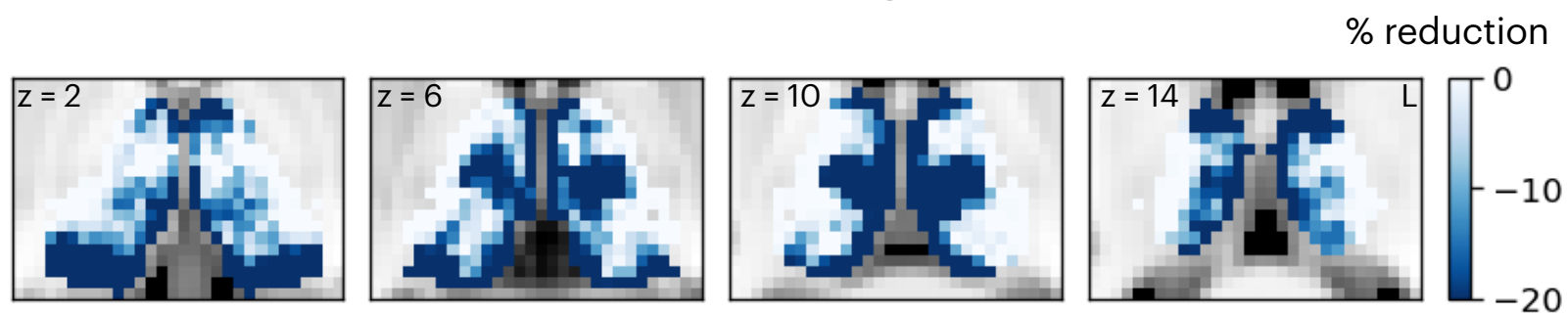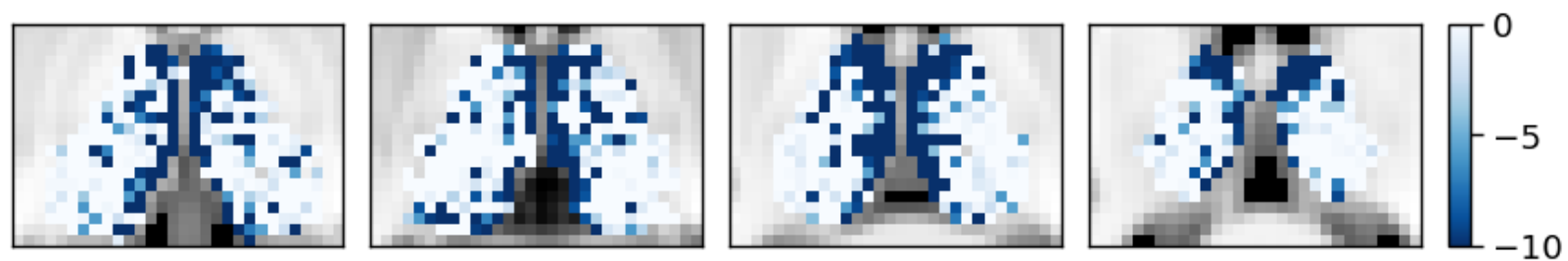projection
to cortex

weight (z scored)
-2.5   2.5

A

$T \times W_t = C$

Thalamic evoked responses

X

Thalamus voxels

Thalamocortical FC (W_t)

Cortical ROIs

=

Predicted cortical evoked responses (C)

Observed cortical evoked responses

Predicted cortical evoked responses

Regions

Tasks

Tasks

Evoked response (a.u.)

Pearson correlation

B

Thalamus
Caudate
Putamen
Pallidus
Hippocampus
Vis
SM
Limbic
DA
CO
DF
FP
Null Model
Uniformed Evoked Model

Dataset
MDTB
N&N

0.0   0.2   0.4

Predicted vs. Observed Evoked Responses

Pearson correlation (r)

C

MDTB

r
0.28

0.1

N&N

r
0.22

0.1

A

Observed RDM   Predicted RDM

Tasks   Tasks

Tasks   Tasks

Kendall's Tau

B

Thalamus
Caudate
Putamen
Pallidus
Hippocampus
Vis
SM
Limbic
DA
CO
DF
FP
Null Model
Uniformed Evoked Model

Dataset
MDTB
N&N

0.0   0.2   0.4
Predicted vs. Observed Evoked Responses

Kendall's Tau
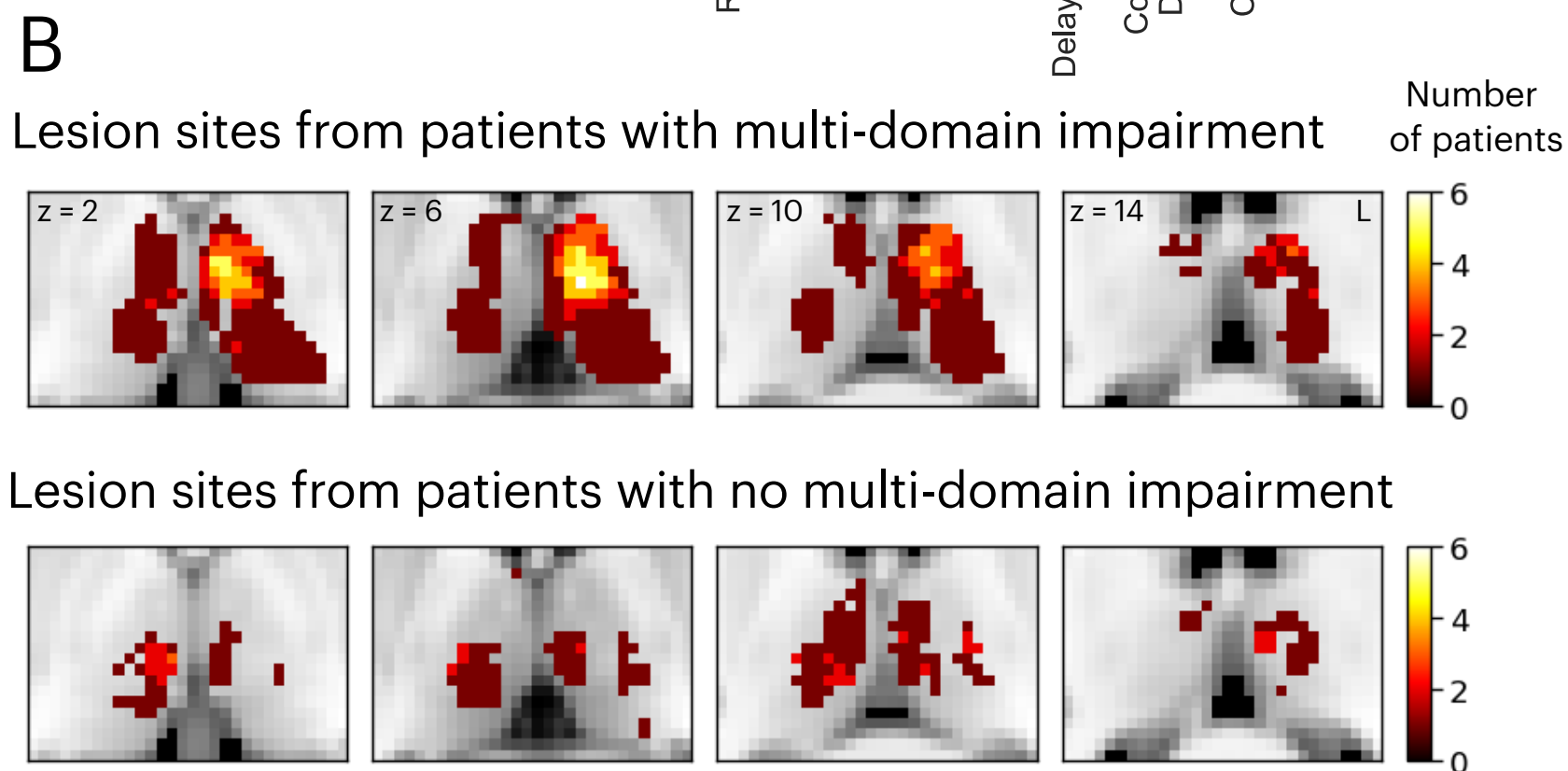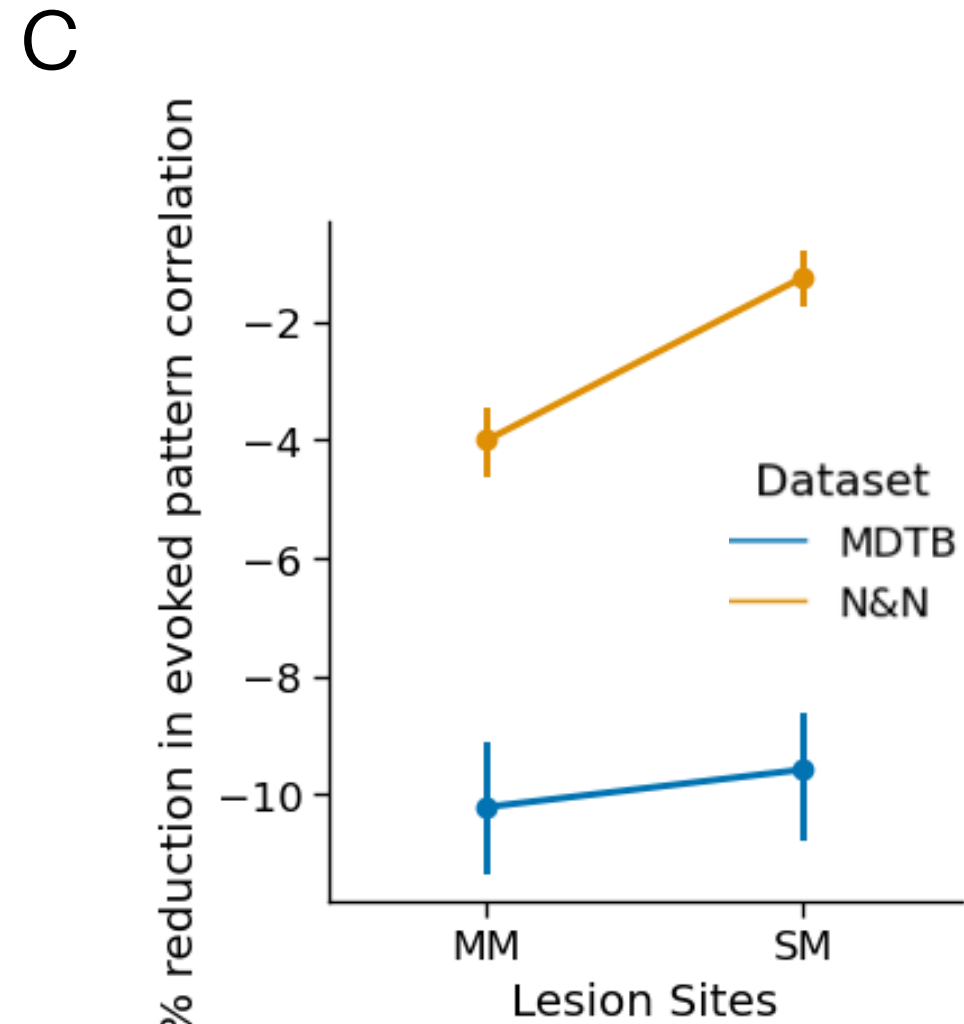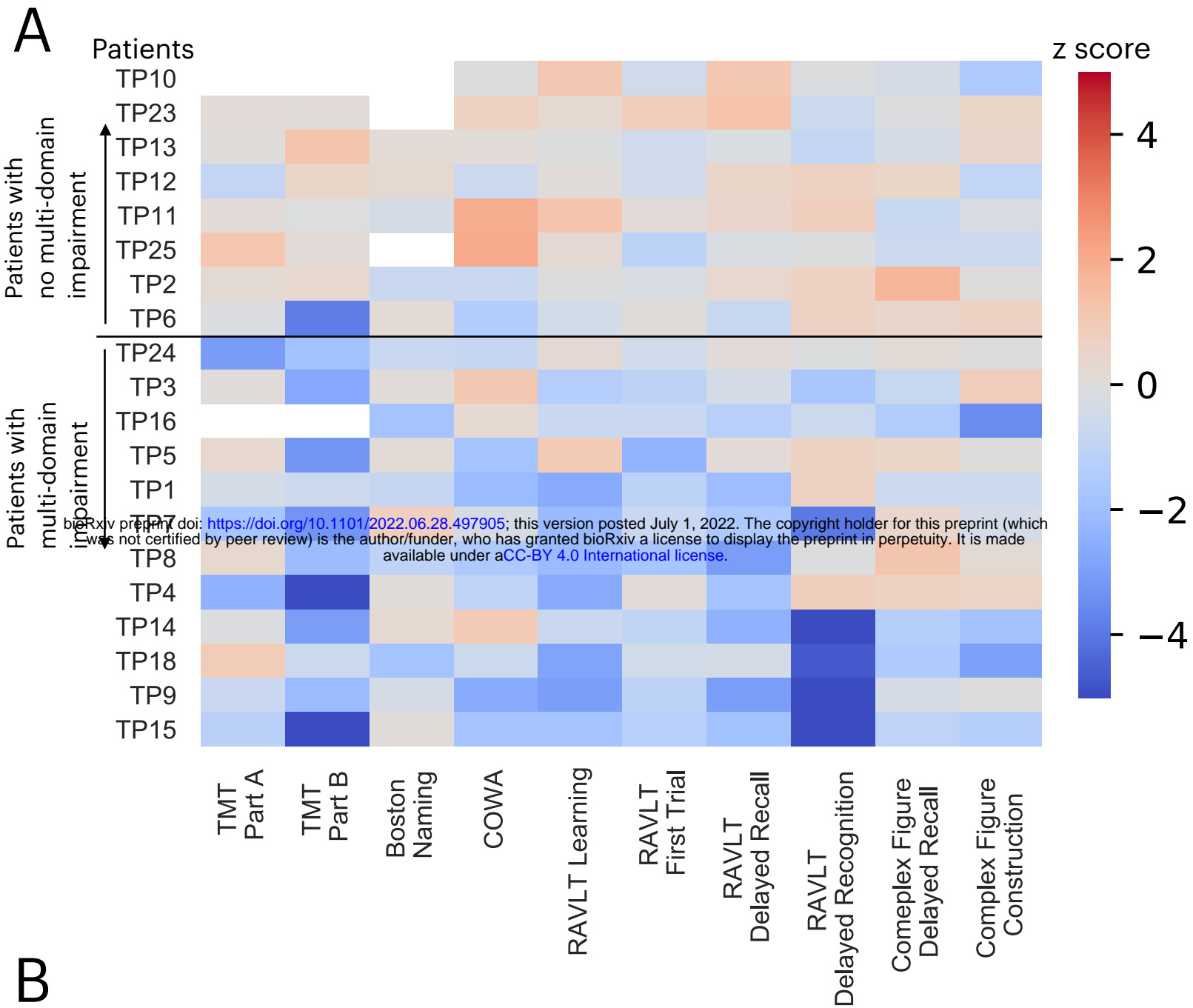
C

Tau
0.27
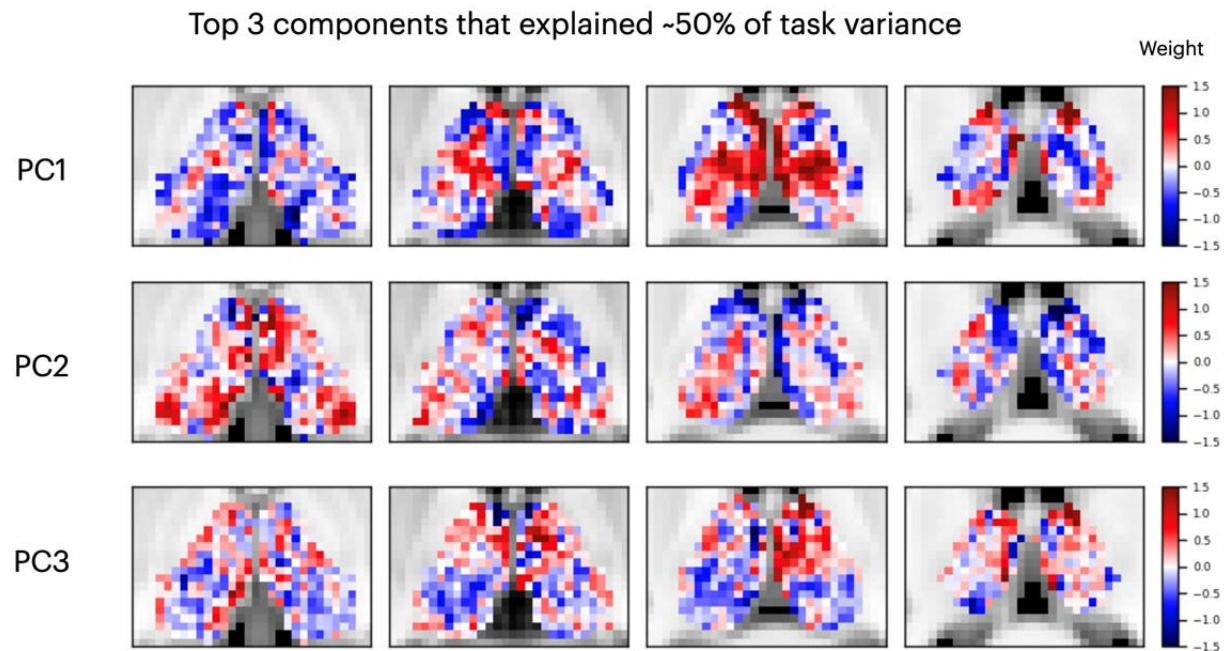
0.1

MDTB

Tau
0.2

0.1

N&N

A

Figure 1 – Figure Supplement 1. Spatial topography of the top three components from the N&N dataset that explained about 50% of the variance in the group averaged task activity matrix.
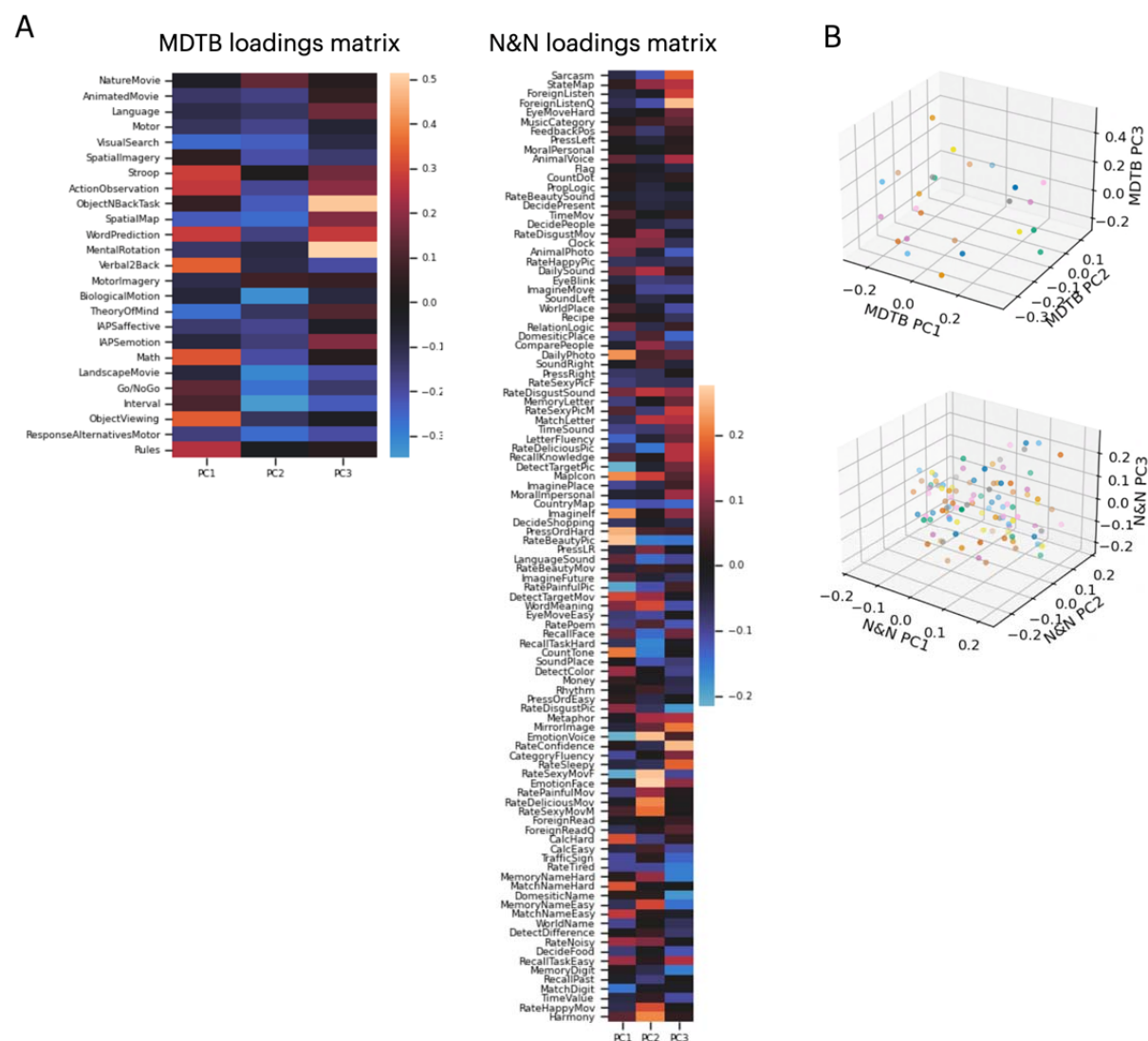
Figure 1 – Figure Supplement 2. Loadings between individual tasks and thalamic activity components. (A) Loadings matrix for the top 3 activity components and individual tasks for both datasets. (B) Low-dimensional embedding of task-evoked responses, plotted by task loadings on each activity component. Each colored dot represents a single task.