



Anatomy and white-matter connections of the precuneus

Onur Tanglay² · Isabella M. Young³ · Nicholas B. Dadario⁴ · Robert G. Briggs¹ · R. Dineth Fonseka² · Vukshitha Dhanaraj² · Jorge Hormovas² · Yueh-Hsin Lin² · Michael E. Sughrue²

Accepted: 26 July 2021

© The Author(s), under exclusive licence to Springer Science+Business Media, LLC, part of Springer Nature 2021

Abstract

Purpose Advances in neuroimaging have provided an understanding of the precuneus' (PCu) involvement in functions such as visuospatial processing and cognition. While the PCu has been previously determined to be apart of a higher-order default mode network (DMN), recent studies suggest the presence of possible dissociations from this model in order to explain the diverse functions the PCu facilitates, such as in episodic memory. An improved structural model of the white-matter anatomy of the PCu can demonstrate its unique cerebral connections with adjacent regions which can provide additional clarity on its role in integrating information across higher-order cerebral networks like the DMN. Furthermore, this information can provide clinically actionable anatomic information that can support clinical decision making to improve neurologic outcomes such as during cerebral surgery. Here, we sought to derive the relationship between the precuneus and underlying major white-matter bundles by characterizing its macroscopic connectivity. **Methods** Structural tractography was performed on twenty healthy adult controls from the Human Connectome Project (HCP) utilizing previously demonstrated methodology. All precuneus connections were mapped in both cerebral hemispheres and inter-hemispheric differences in resultant tract volumes were compared with an unpaired, corrected Mann–Whitney U test and a laterality index (LI) was completed. Ten postmortem dissections were then performed to serve as ground truth by using a modified Klingler technique with careful preservation of relevant white matter bundles. **Results** The precuneus is a heterogenous cortical region with five major types of connections that were present bilaterally. (1) Short association fibers connect the gyri of the precuneus and connect the precuneus to the superior parietal lobule and the occipital cortex. (2) Four distinct parts of the cingulum bundle connect the precuneus to the frontal lobe and the temporal lobe. (3) The middle longitudinal fasciculus from the precuneus connects to the superior temporal gyrus and the dorsolateral temporal pole. (4) Parietopontine fibers travel as part of the corticopontine fibers to connect the precuneus to pontine regions. (5) An extensive commissural bundle connects the precuneus bilaterally. **Conclusion** We present a summary of the anatomic connections of the precuneus as part of an effort to understand the function of the precuneus and highlight key white-matter pathways to inform surgical decision-making. Our findings support recent models suggesting unique fiber connections integrating at the precuneus which may suggest finer subsystems of the DMN or unique networks, but further study is necessary to refine our model in greater quantitative detail.

Keywords Precuneus · Medial posterior parietal · Anatomy · Tractography · White matter · DSI

✉ Michael E. Sughrue
sughruevs@gmail.com

¹ Department of Neurosurgery, University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA

² Centre for Minimally Invasive Neurosurgery, Suite 19, Level 7 Prince of Wales Private Hospital, Barker Street, Randwick, Sydney, NSW 2031, Australia

³ Cingulum Health, Sydney, NSW, Australia

⁴ Robert Wood Johnson School of Medicine, Rutgers University, New Brunswick, NJ, USA

Introduction

The precuneus (PCu) constitutes the posterior region of the medial parietal cortex. There have been limited studies on the PCu prior to the past decade due to its complex anatomy and difficult access during dissection, buried within the interhemispheric fissure deep to the sagittal sinus and bridging veins (Cavanna & Trimble, 2006). However, recent advancements in neuroimaging abilities have facilitated greater insight into the structure and function of this deep brain region, and provided improved neural connectivity

studies (Caspers & Zilles, 2018; Cavanna & Trimble, 2006; Cunningham et al., 2017; Skandalakis et al., 2020; J. Wang et al., 2019) and updated whole-brain parcellation maps (Baker et al., 2018; Glasser et al., 2016). Functionally, the precuneus is involved diverse roles including visuospatial and visuomotor integration, autobiographical memory, and self-awareness (Zhang & Li, 2012). Part of the PCu also serves as a core hub of the default mode network (DMN), facilitating the integration of resting state processes, attention regulation, and higher-order cognition (Utevsky et al., 2014).

The posteromedial parietal cortex is rarely injured in isolation, accounting for the few number of focal lesion studies in this region (Cavanna & Trimble, 2006). Additionally, resection of the PCu following focal seizures or tumor invasion is generally thought to be well-tolerated. It is however likely that any deficits which may develop are not tested due to a limited understanding of the function and connectivity of this area in the clinical setting. The PCu's involvement in a variety of cognitive processes and role in the default mode network necessitates a more detailed study of its major cortico-cortical connections to aid in intraoperative decision making and avoid damage to tracts which facilitate its extensive connectivity. A great deal of discussion has posited unique subsystems within the default network to support specialized functions, such as with memory which may involve connections from temporal areas integrating at the PCu and posterior cingulate cortex (Buckner et al., 2008). However, others argue for the complete segregation of parts of the PCu from the DMN into its own specialized network adjacent to the DMN (Gilmore et al., 2015; Yang et al., 2014). Detailed structural tractographic analyses of the PCu with adjacent cerebrum may provide clarity on the association of distinct parts of this cortical region with higher-order networks to support its implication in a diverse range of neuro-behavioral and motor functions. A clinically actionable anatomical study may therefore improve surgical outcomes by better understanding these cortical connections (Robert G. Briggs et al., 2021).

This study demonstrates the anatomic organization of the major white matter bundles connecting to the PCu in relation to adjacent structures. Diffusion spectrum imaging (DSI)-based tractography is used to characterize the connectivity of the networks associated with the PCu, validated by gross anatomical dissection as ground truth. The connections derived from this study may be of use to neurosurgeons in preserving neural networks dependent on connections in this brain region.

Methods

Defining the region of interest

Uniform anatomic boundaries were applied to our dissections and used for manually generated ROIs in fiber tracking. The PCu is situated between the triangular cuneus on the medial occipital lobe posteriorly, and the paracentral lobule anteriorly (Cavanna & Trimble, 2006). It is delineated anteriorly by the ramus marginalis of the cingulate sulcus (RC), inferiorly by the subparietal sulcus (SS) and posteriorly by the medial portion of the parieto-occipital sulcus (PO) (Pereira-Pedro & Bruner, 2016). These boundaries are shown on a dissected brain in Fig. 1. These boundaries are variable between individuals. The parieto-occipital fissure is either straight, T-shaped or exhibits three branches, extending to the upper bend of the calcarine sulcus or more anteriorly (Pereira-Pedro & Bruner, 2016). The subparietal sulcus is often H-shaped with one to three branches, and also shows immense interindividual variability (Gürer et al., 2013; Pereira-Pedro & Bruner, 2016).

Structural tractography

Publicly available imaging data from the Human Connectome Project (HCP) were obtained for this study from the HCP database (<http://human-connectome.org>, release Q3). Tractographic analyses were completed utilizing methods which have been previously demonstrated with great reproducibility by our team on numerous other cortical regions

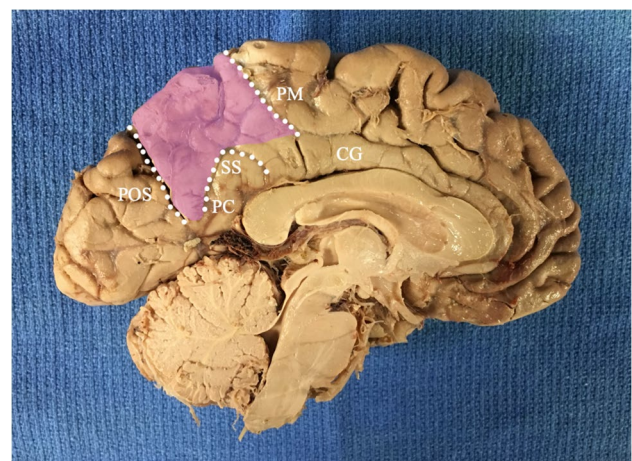


Fig. 1 Superficial anatomy of the precuneus from a midsagittal section. The dotted lines delineate the borders of the precuneus, which is highlighted in pink. RC, ramus marginalis of the cingulate sulcus; PO, parietooccipital sulcus; SS, subparietal sulcus; CG, cingulate gyrus

(R. G. Briggs et al., 2019; Burks et al., 2017a, b, 2018; Lin et al., 2021; Palejwala, et al., 2020a, b; Palejwala et al., 2020a, b; Sheets et al., 2020). Diffusion imaging with corresponding T1-weighted images from 10 healthy, unrelated subjects were analyzed during fiber tracking analysis (Subjects IDs: 100,307, 103,414, 105,115, 110,411, 111,312, 113,619, 115,320, 117,112, 118,730, 118,932). A multi-shell diffusion scheme was used, and the b-values were 1000, 2000, and 3000s/mm². Each b-value was sampled in approximately 90 directions. The in-plane resolution was 1.25 mm. The diffusion data were reconstructed using generalized q-sampling imaging with a diffusion sampling length ratio of 1.25 (Yeh et al., 2010).

Upon registering all brains to the MNI coordinate space, tractography was performed in DSI Studio (Carnegie Mellon) using a region of interest (ROI) approach to initiate fiber tracking from a user-defined seed region (Martino et al., 2013). A two-ROI-approach was used to isolate tracts (Kamali et al., 2014).

Voxels within each ROI were automatically traced with a maximum angular threshold of 45°. When a voxel was approached with no tract direction or a direction change of greater than 45°, the tract was halted. Tractography was terminated after reaching a maximum length of 800 mm. In some instances, exclusion ROIs were placed to exclude spurious tracts that were not involved in the white matter pathway of interest.

Inter-hemispheric comparisons

Tracts were identified in both hemispheres for all regions of the PCu, processing systematically anteriorly to posteriorly. Possible inter-hemispheric differences were analyzed by comparing resultant tract volumes from the left and right hemispheres within individuals using the corrected, non-parametric, unpaired Mann–Whitney U-test. A laterality index was also completed using the formula (right average tracts–left average tracts)/(right average tracts+left average tracts) (Thiebaut de Schotten et al., 2011). Given the precuneus is known as a very heterogeneous region, group averages within our entire sample (n=20) were also compared with just those who demonstrated the cortical connections of interest (Table 1).

Post-mortem dissection

Major tracts originating from the PCu found in tractography were validated using gross anatomical dissections as ground truth (Burks et al., 2017a, b; Catani et al., 2012). Postmortem dissections were performed using a modified Klingler technique (Koutsarnakis et al., 2015). Ten hemispheres were used for this study, obtained from our institution's Willed Body Program with approval of the state's anatomical board. All specimens were donated by individuals who died from causes unrelated to intracranial pathology. The cadaveric

Table 1 Connections of the precuneus in both cerebral hemispheres

Cortical regions	Number of subjects identified with connection (/20)	Average connections weighted by <i>all subjects</i> (L+R/2)	Average connections weighted by only <i>identified</i> subjects				Connection type	
			Average connections (L+R/2)	R	L	LI		P-value
PCu to PHG	R=11 L=13	96	157	125	188	-0.20	P=0.66	Cingulum (CB-V)
PCu to SFG	R=10 L=15	89	139	61	116	-0.31	P=0.11	Cingulum (CB-III and CB-IV)
PCu to anterior cingulate	R=8 L=9	69	182	268	95	0.48	P=0.48	Cingulum (CB-I)
PCu to SPL and occipital cortex	R=20 L=20	1950	1950	1889	2011	-0.03	P=0.46	U-fibers
PCu to STG	R=14 L=12	29	45	43	47	0.04	P=0.87	Middle Longitudinal Fasciculus
PCu to Brainstem	R=12 L=10	250	472	656	287	-0.39	P=1.00	Parietopontine
Left PCu to Right PCu	R/L=13	458	703					Commissural

Average connections were compared within the entire study sample (n=20) and just with those who demonstrated the connections of interest for further analyses in identified subjects. Further analyses were completed solely on those with the connections of interest. A lateralization index was calculated as (right average tracts—left average tracts)/(right average tracts+left average tracts). A negative value indicates a leftward asymmetry in connectivity and positive values indicate a rightward asymmetry. Inter-hemispheric differences were compared with a corrected, unpaired Mann–Whitney U test. *L* left; *LI* lateralization index, *PCu* precuneus, *PHG*, parahippocampal gyrus, *R* right, *SPL* superior parietal lobe, *STG* superior temporal gyrus

brains were obtained after embalming and further fixed in 10% formalin for at least 3 months after removal from the cranium. Up until the time of dissection, the pia-arachnoid membrane was left attached.

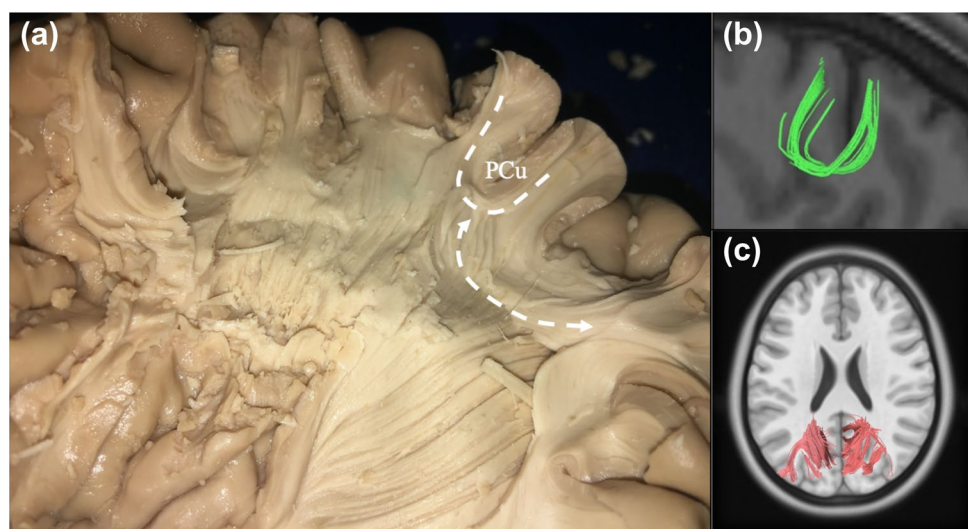
After fixation with formalin, specimens were rinsed with water for 2 days, and then frozen at -10°C for 8 h to disrupt the white matter. After thawing, dissection of the “freeze-fractured” specimens began with removal of meninges and identification of cortical anatomy, including gyri and sulci. Relevant cortical areas were identified first. Starting superficially, they were then peeled back to reveal white-matter areas of interest, and care was taken to leave cortical areas corresponding to white-tracts of interest intact to preserve their relationship with one another. Tracts were dissected with blunt instruments to avoid disrupting the natural tract anatomy with care taken not to create spurious tracts. Photographs were taken at each stage in the dissection, and spatial relationships were recorded. All PCu tracts were dissected in both hemispheres.

Results

Short-range association fibers

A dense network of U-fibers within the PCu and local fibers to the surrounding superior parietal lobule were present. There were also fibers extending from the ventromedial regions of the PCu to the occipital cortex, mainly the primary visual area, travelling over the top of the optic radiation. To further characterize these connections is beyond the scope of this study, however some examples on tractography and dissection are shown in Fig. 2.

Fig. 2 Short association fibers of the precuneus. U-shaped fibers, dotted line in gross dissection (a), and green tracts in (b), connect adjacent gyri. There are also fibers connecting the precuneus to the occipital cortex. Some connections are shown by the dotted arrow in gross dissection (a), while tractography (c) demonstrates fibers from the precuneus to the occipital cortex travelling over the optic radiation. PCu, precuneus



Long range association fibers

Cingulum Four subcomponents of the cingulum bundle were identified. The CB-I fibers originate from the ventral PCu, coursing anteriorly along the body of the CC before arching around the genu of the CC and terminating in the anterior cingulate and orbito-frontal cortices. CB-III was the largest CB bundle identified, originating from a large portion of the ventral PCu and terminating along the medial aspect of the superior frontal gyrus. CB-IV extends from the PCu to more anterior frontal regions, including the premotor and supplementary motor areas. CB-V fibers originate from the PCu and terminate in the parahippocampal gyrus. These CB segments are shown in Figs. 3 and 4.

Middle Longitudinal Fasciculus MdLF fibers stem from the PCu and superior parietal lobule, course antero-inferiorly behind the splenium of the CC to terminate in the dorsolateral temporal pole and the superior temporal gyrus, particularly in regions surrounding Heschl's gyrus (Fig. 5). The volume of this tract and the extent of its reach to the temporal pole varied between individuals.

Parietopontine Fibers These fibers arise from the PCu and follow the course of the corona radiata to descend within the posterior limb of the internal capsule to terminate in the brainstem, mainly the pons (Fig. 6). Characterizing these connections in greater detail is beyond the scope of this study.

Callosal Fibers The left and right PCu are connected via a dense callosal fiber bundle. These commissural fibers initially descend rostroventrally lateral to the orthogonal CB fibers, before curving ventral to the CB to project through the splenium and isthmus of the corpus callosum, connecting the PCu bilaterally (Fig. 7).

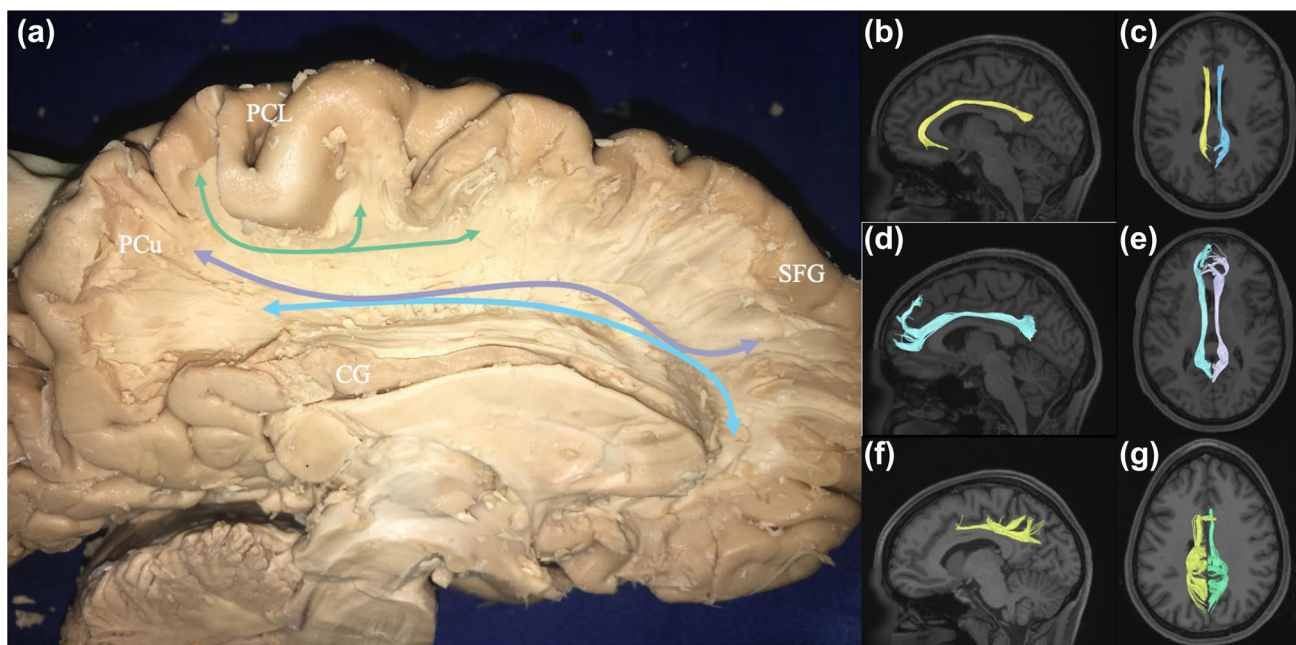


Fig. 3 Three distinct cingulate bundle fibers arising from the precuneus. CB-I, depicted by the light blue arrow on dissection (a) and the sagittal (b) and axial (c) views on tractography, travels over the corpus callosum to connect the precuneus to the orbitofrontal and anterior cingulate cortices. CB-III, shown by the green arrow in (a) and the sagittal (d) and axial (e) views on tractography, travels from the

precuneus to terminate along the medial aspect of the superior frontal gyrus. CB-IV, the green arrow in (a), and shown in sagittal (f) and axial (g) views on tractography, connects the precuneus to more anterior cortical regions, including the premotor and supplementary motor areas. PCu, precuneus; PCL, paracentral lobule; SFG, superior frontal gyrus; CG, cingulate gyrus

Laterality indices

Table 1 lists the volumetric laterality indices comparing the CBs, MdLF, and parietopontine fibers. These cortical connections were present in most individuals and were mostly left-lateralized. However, no significant differences bilaterally were noted ($p > 0.05$).

Discussion

The connections of the precuneus have previously received inadequate attention, especially in terms of surgical and gross anatomy. In this study, we aimed to fill this void by demonstrating the connections of the PCu in relation to gross anatomical structures. An improved understanding of the PCu and its cortico-cortical connectivity will better inform clinical pathologies which may involve precuneal injuries, such as in Alzheimer's Disease (He et al., 2020), epilepsy (Harroud et al., 2017), depression (Cheng et al., 2018), and Parkinson's Disease (Thibes et al., 2017).

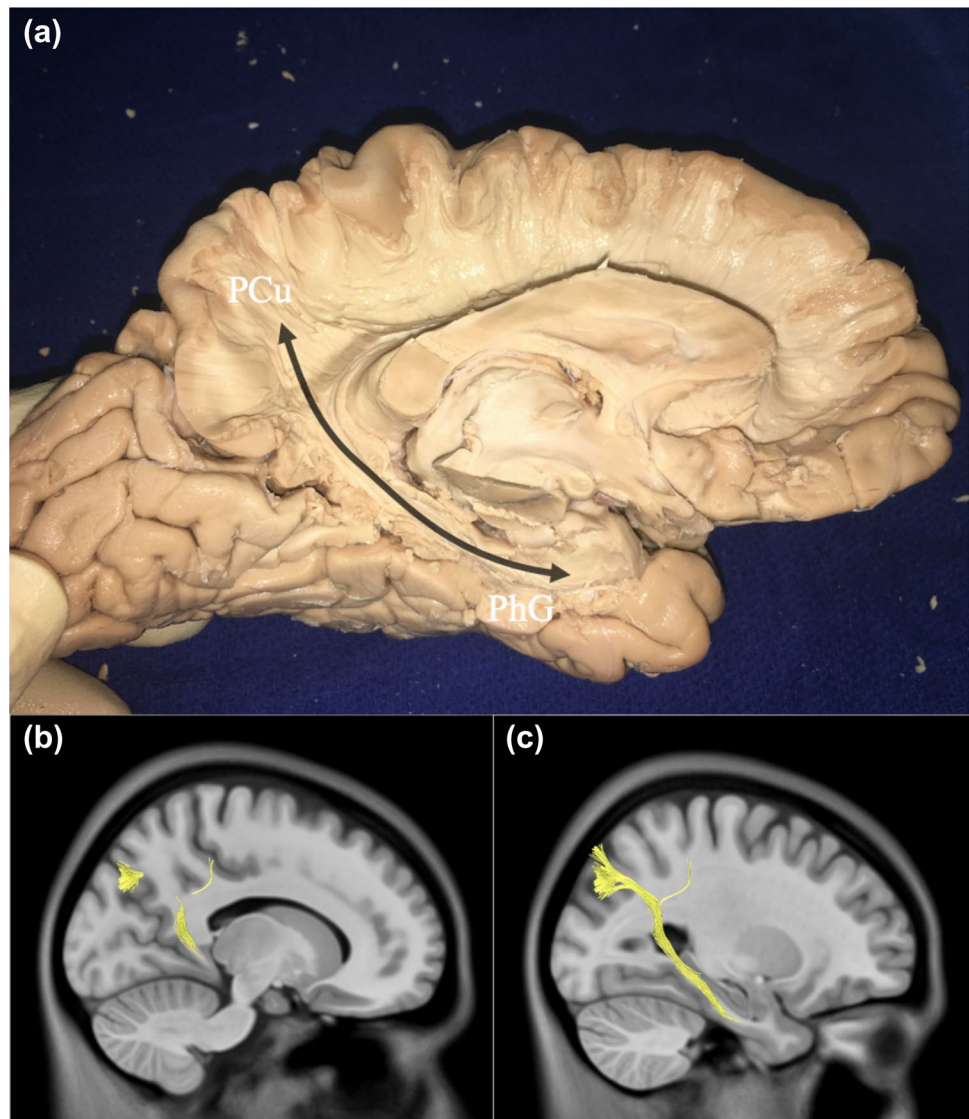
Several tractographic studies of the CB and MdLF have identified the PCu as an important region and highlighted its connections with the frontal, parietal and temporal cortices, consistent with the findings of this study (Kalyvas et al., 2020; Skandalakis et al., 2020; Wu, Sun, Wang, Wang, &

Ou, 2016). A majority of the understanding of the connectivity of the posteromedial parietal lobe is however largely derived from axonal tracing studies using horseradish peroxidase in the macaque brain, whose posteromedial cortex most closely resembles *Homo sapiens* compared to other primates (Leichnetz, 2001). In addition to the aforementioned cortical areas, these studies linked the PCu to several subcortical regions including the caudate nucleus and putamen, claustrum and several brainstem structures such as the superior colliculus, pretectal area and the nucleus reticularis tegmenti pontis (Leichnetz, 2001). Although investigating connections with subcortical structures was beyond the scope of this study, fibers to the brainstem were identified but their endpoints were not characterized. In addition, connections to the dorsal thalamus have also been reported (Cunningham et al., 2017), though this was not observed.

The cingulum bundle and middle longitudinal fasciculus

The MdLF was first identified in humans as a pathway connecting the angular gyrus and the superior temporal gyrus, with little understanding of its function (Menjot de Champfleury et al., 2013). Early studies suggested the bundle served a combination of roles traditionally associated with the arcuate fasciculus (Makris et al., 2013), while

Fig. 4 The parahippocampal cingulum. CB-V fibers connect the precuneus to the parahippocampal gyrus, travelling posterior to the splenium of the corpus callosum. This tract is shown on dissection (**a**) by the black arrow, and on tractography through a sagittal series in (**b**) and (**c**). PCu, precuneus; PhG, remnants of the parahippocampal gyrus, which has been removed

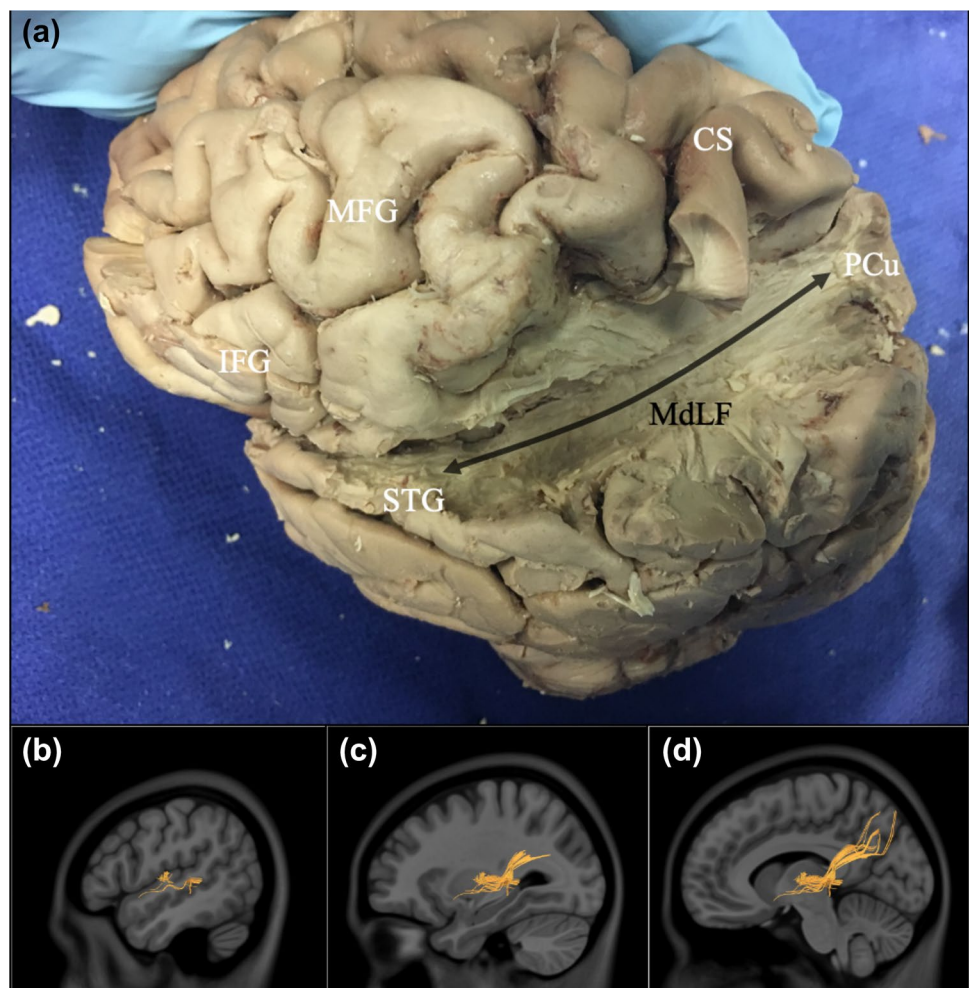


others proposed that it participated in dorsal and ventral processing streams (Saur et al., 2008). Its role in language processing is however doubted due to the lack of a strong connection between the superior temporal gyrus and inferior parietal lobule through the MdLF (Wang et al., 2013), the inability of direct stimulation and cortical resection of the MdLF to produce language deficits (De Witt Hamer et al., 2011), though these only focused on the anterior CB, and a lack of lateralization observed in other language pathways (Kalyvas et al., 2020). Recently the MdLF has been mapped into three segments, with MdLF-I connecting the temporal pole and superior temporal gyrus (STG) to the PCu and the superior parietal lobule, identified in this study; MdLF-II connecting the temporal pole (TP) and STG with the parieto-occipital area; and MdLF-III connecting the TP to the occipital lobe via the angular gyrus (Kalyvas et al., 2020). The

proximity of these proposed fibers question whether such stratifications can be made, and whether these are clinically useful. Attempts at further characterizing the MdLF may however aid in illuminating its function. Kalyvas and colleagues (Kalyvas et al., 2020) suggest that its connectivity is indicative of auditory function, and the integration of auditory and visual information. Our findings support this; however, it is likely the MdLF is involved in more functions in line with the variety of roles of the PCu, including facilitating possible connections of the PCu with structures around the temporal pole, such as the amygdala. Indeed, studies have demonstrated functional connectivity between the PCu and amygdala (Ferri et al., 2016; Wei et al., 2018), though further connectivity studies are required to substantiate this.

The cingulum bundle fibers were classified according to a recent study which grouped the cingulum bundle in

Fig. 5 The middle longitudinal fasciculus. Fibers, represented on dissection (a) by the black arrow, arise from the precuneus and course laterally and rostroventrally to terminate at the upper bank of the superior temporal gyrus, and the dorso-lateral temporal pole. The tract is shown on tractography in sagittal series in (b)–(d). MdLF, middle longitudinal fasciculus; PCu, precuneus; STG, superior temporal gyrus; CS, central sulcus; MFG, middle frontal gyrus; IFG, inferior frontal gyrus



the human brain into five segments, based on the same segmentation in the monkey brain (Wu et al., 2016). Four of these segments were relevant to the PCu and they were identified on tractography and fiber dissection. The

functional correlates of the CB are however not well characterized, though its connectivity and several functional studies suggest a predominant role in “limbic” and higher-order functions (Bubb et al., 2018). The more anterior

Fig. 6 Parietopontine fibers. These fibers, depicted by the black arrow on dissection (a) and on tractography in sagittal (b) and coronal (c) views, connect the precuneus to pontine regions. Fibers travel along the corona radiata, the posterior limb of the internal capsule, and the cerebral peduncle to terminate predominantly in the pons. PCu, precuneus; CP, cerebral peduncle

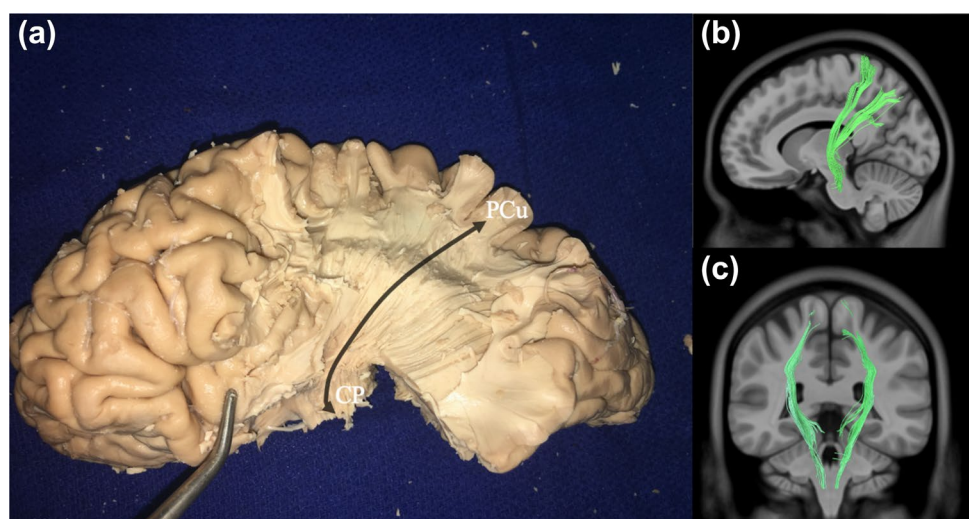
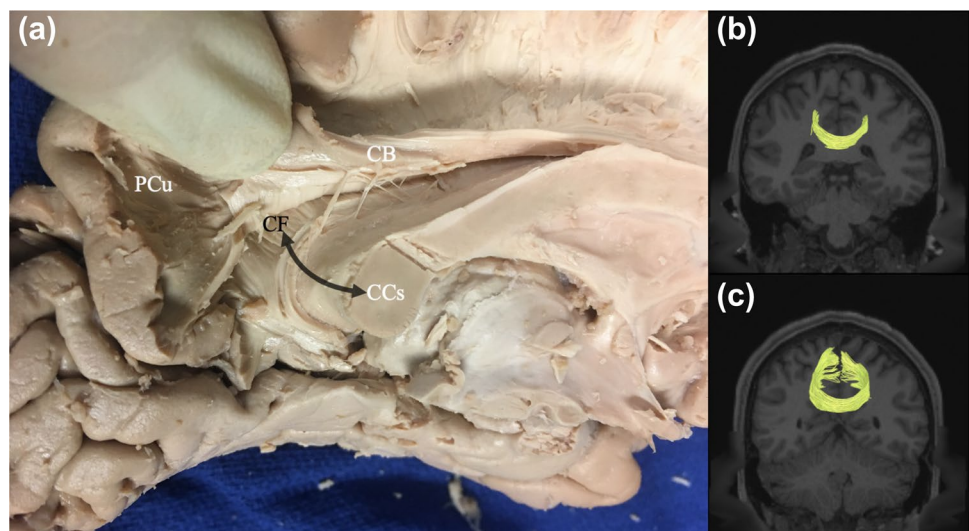


Fig. 7 Callosal fibers. A dense commissural fiber bundle, depicted by the black arrow on dissection (a) and coronal views on tractography (b)-(c), connects the left and right precuneus. These fibers descend adjacent to the perpendicular cingulum and curve ventral to it to project to the contralateral precuneus through the splenium and isthmus of the corpus callosum. PCu, precuneus; CB, cingulum bundle; CCs, splenium of the corpus callosum; CF, callosal fibers



portions are linked to emotion, while posterior segments are associated with memory, due to connections to the parahippocampal gyrus (Wu et al., 2016). The following will review some of the functions of the PCu and link these to the tracts identified.

Precuneus and resting state

Resting state networks are large-scale brain networks which are active during passive states (Cunningham et al., 2017). The default mode network has been of particular interest, comprising regions within the PCu and posterior cingulate cortex, the medial prefrontal cortex and the temporoparietal junction (Buckner et al., 2008). Anatomically, these connections are facilitated by the CB-I and local fibers connecting areas of the parietal cortex. Previous models generally suggest the DMN exhibits increased activation during rest and some specific tasks such as autobiographical memory, while its activity decreases during most active or novel tasks (Raichle et al., 2001). Recent studies have however shown that this model is too simplistic, especially for the PCu and posterior cingulate cortex (PCC), which display distinct connectivity to the rest of the DMN (Utevsky et al., 2014). Specifically, the ventral PCu/PCC are functionally connected to the central executive network (CEN) during difficult memory tasks, rather than the deactivated DMN, while the dorsal PCu/PCC deactivates similar to the DMN (Leech et al., 2011). Other studies have demonstrated that the connectivity of the PCu with the DMN depends on the activity and the subject's level of engagement,

and a more comprehensive review of these isolated studies is required to make further hypotheses on the function of the PCu (Anderson et al., 2011; Andrews-Hanna et al., 2014; Che et al., 2014; Utevsky et al., 2014; Xu et al., 2016). Furthermore, the PCu has one of the highest resting metabolic rates within the DMN and selectively deactivates in sleep, anesthesia, and a vegetative state (Cavanna, 2007; Utevsky et al., 2014). It therefore appears to play a key role in conscious information processing beyond its role in the DMN and likely modulates the interaction between cognition and attentional states.

Precuneus and episodic memory

While previous research has suggested the role of the medial temporal lobe in episodic memory, emerging research has revealed the significance of the PCu in episodic memory retrieval, as episodic memory is incomplete without the sense of self, preserved as autobiographical memory (Lundstrom et al., 2005). Specifically, it is the awareness of subjective time linked to personal experiences, referred to as 'autonoetic consciousness' which underlies the role of the PCu in episodic memory retrieval (Sreekumar et al., 2018). Several fMRI studies display increased activity in the PCu during retrieval of context-rich memories (Kwok et al., 2012; Wagner et al., 2005). The key role of the PCu in retrieval of vivid subjective experience is supported by the discovery that it is affected early in Alzheimer's Disease when memory of time, people and places is obfuscated (Scheff et al., 2013; Yokoi et al., 2018).

Anatomically, it is likely that the cingulum bundle facilitates many of these tasks. Of interest, the parahippocampal cingulum (CB-V) is thought to act as a control pathway supporting several cognitive functions, including the transfer of visuospatial, facial and mnemonic cues from the medial temporal area to the PCu (Skandalakis et al., 2020). It is therefore unsurprising that the integrity of the parahippocampal cingulum is in AD and is a target of studies for early diagnosis (Dalboni da Rocha et al., 2020; He et al., 2020; Mito et al., 2018). While the functional significance of this bundle has not yet been clinically validated, awareness of this tract is useful during brain surgery involving areas close to the adjacent ventricular atrium.

The role of the PCu and the rest of the parietal cortex in memory encoding is unclear. While some studies report that deactivation of these regions during encoding exhibits better retrieval, other studies have demonstrated positive memory effects upon activation of the dorsal PCu (Brodt et al., 2016; Hebscher et al., 2020; Schott et al., 2019). It is possible that the dorsal PCu plays a distinct role in encoding of spatial information, perpetuating a functional distinction between the ventral and dorsal PCu which is discussed in greater detail below (Schott et al., 2019).

Precuneus and visuospatial processing

The parietal cortex is crucial in the integration of motor and sensory signals to decide movements in space (Whitlock, 2017). The PCu is believed to contribute to the coordination of spatially guided behavior, including spatial relations for body movement and visual attention (Cavanna & Trimble, 2006; Zhang & Li, 2012). One study found that the dorso-rostral PCu along with the anterior cingulate cortex were activated during spatially-complex bimanual coordination (Wenderoth et al., 2005). Furthermore, several studies have identified the PCu as the human homologue to the monkey parietal reach region (PRR) with activity dedicated to goal-directed reaching behavior (Filimon et al., 2009; Gertz & Fiehler, 2015; Hwang et al., 2012). Damage to the PRR in the monkey results in the reach errors seen in optic ataxia, a rare condition in humans with impairment in the coordination of visually guided hand movements (Andersen et al., 2014). The PCu is however not the only area impacted, and in some cases lesions do not extend deep into the parietal cortex, warranting further study (Andersen et al., 2014; Hwang et al., 2012; Vindras et al., 2016). Another study utilized repetitive transcranial magnetic stimulation (rTMS) over the right PCu in healthy adults and achieved a neglect-like effect (Mahayana et al., 2014), again suggesting a role in spatial attention which requires further investigation.

Anatomically, the connections of the PCu to other parts of the parietal cortex, the frontal motor areas, and the occipital cortex, along with previously mentioned connections to

several “oculomotor” brainstem regions may be responsible for facilitating its activity in visuospatial imagery.

Defining the network association of the precuneus

As discussed in great deal above, the precuneus is implicated in a diverse range of neuro-behavioral and motor behaviors likely due to its heterogenous connectivity both across adjacent cortical regions as well as from various divisions within the precuneus itself. Given that differences have been previously proposed on the functional roles of the anterior versus posterior PCu, such as in self-centered mental imagery strategy (anterior PCu) compared to episodic memory retrieval (posterior PCu), there is great discussion on whether a dissociation of the dorsal part of the PCu should exist from its typical association with the larger DMN network in general (Buckner et al., 2008; Cavanna & Trimble, 2006; Gilmore et al., 2015; Greicius et al., 2003; Yang et al., 2014). Early meta-analyses characterize a default network of cortical regions which show decreased activity on PET studies during passive viewing of a stimulus, consisting of the posterior cingulate and precuneus regions, left and right inferior parietal cortex, left dorsolateral frontal cortex, left lateral inferior frontal cortex, left inferior temporal gyrus, a strip of medial frontal regions running along a dorsal–ventral axis, and the right amygdala (Greicius et al., 2003). While similar regions were identified in the current study with grossly different methodology, we found strong connections between the dorsal PCu with temporal regions compared to more anterior PCu connections which may support the possibility of selective association of only part of the PCu with the DMN, namely the anterior PCu. A portion of MdLF fibers identified (MdLF-I) connected the PCu with the temporal pole and STG while parahippocampal cingulum (CB-V) fibers connected the medial temporal area to the PCu.

If separated from the DMN, the precuneus may be involved in a separated “parietal memory network (PMN)” which deactivates to novel stimuli while activating to familiar stimuli (Gilmore et al., 2015). This possible network has been characterized to include cortices which flank the DMN, including the PCu, part of the middle/posterior cingulate-cortex, posterior IPL and dorsal angular gyrus. Indeed, temporal connections identified in this study support hypotheses on the retrieval of previously stored information that are relayed from cortices around the parahippocampal gyrus (CB-V) and temporal pole (MdLF-I) to the dorsal PCu. The current study found that these connections were present bilaterally, which has not been demonstrated in great detail previously (Gilmore et al., 2015). Elsewhere, the precuneus has been similarly separated from the DMN in a precuneus-dorsal posterior cingulate cortex network that may reflect age-related decline (Yang et al., 2014).

Interestingly, a PCu-dPCC network may appear functionally distinct from the DMN in younger individuals while eventually demonstrating functional co-activation and integration with the greater DMN in late-adulthood, thus illustrating different origins on the two networks.

While not mutually exclusive from the above hypotheses, the DMN may likely instead be characterized as a series of subsystems which integrate in key DMN hub areas from different cortices based on the functions required in a given moment, rather than just thinking of the DMN as a single monosynaptically connected network (Buckner et al., 2008). In this context and supported by findings from the current study, one subsystem of the DMN possibly specialized for memory retrieval is the *medial temporal lobe subsystem* (Buckner et al., 2008). Such a system including temporal connections to the posterior PCu hub would provide information on previous experiences from autobiographical memory to plan for future cognitive and motor actions. Nonetheless, further identification and characterization of structural and functional coupling of cortical regions with hub areas in the DMN in specialized subsystems is of the utmost importance and requires further clarity due to the heterogeneous brain disorders and cognitive functions implicating the DMN.

Limitations and future directions

Connectomic based studies provide the opportunity to create anatomically precise network models that support discussions of functional significance with strong prediction values (Baker et al., 2018; Finn et al., 2015). Through tractographic analyses, these models can discriminate specific structural connections that are difficult to appreciate with the human eye and can provide clinically actionable anatomic information that can guide cerebral surgery to improve neurologic outcomes (Briggs et al., 2021). Such structural analyses are necessary when discussing the connectivity and clinical relevance of diversely implicated regions such as the precuneus in the current study. Our findings support a possible memory network integrating at the posterior precuneus mediated by temporal connections which may serve as a subsystem within the DMN or may indeed possibly characterize a unique, adjacent network altogether (Buckner et al., 2008; Gilmore et al., 2015; Yang et al., 2014).

However, it is important to note that the current study aimed to present qualitative, descriptive analysis that provides anatomically actionable data and supports further discussion on their functional relevance or segregation. Tractography is limited in its quantitative measurements due to individual differences seen

in brain connectivity that may be difficult to appreciate with group-average analyses as employed in the current study. However, similar samples sizes and methodology have been reiteratively refined and applied to other cortical regions with by our team great success (Baker et al., 2018; Briggs et al., 2019; Burks et al., 2018; Lin et al., 2021; Palejwala et al., 2020a, b; Sheets et al., 2020). The certain threshold in number of components, seeds, or subjects that may be necessary in a data-driven analysis to appreciate the “dissociation” in subsystems of the DMN or precuneus connectivity is uncertain and other studies which argue for the separation of the precuneus from the DMN suggest that their findings are often robust to the number of ICA components (Yang et al., 2014). Still, our findings should be appreciated within the scope of our current limitations and future studies should look to investigate the connectivity of the precuneus with more rigorous quantitative analyses across a heterogeneous sample of individuals. The current findings highlight the heterogeneous connections of the precuneus that may reside in unique subsystems or separated networks in order to support diverse functional roles or contribute to pathophysiological states.

Conclusions

This study highlights the major white-matter pathways of the PCu and its underlying connections. We present a summary of the relevant clinical anatomy of this region as part of an effort to better understand its function and inform surgical decision-making. In support of previous studies, posterior regions of the PCu demonstrated unique connections with temporal areas which may explain its role in the retrieval of autobiographical information to plan for future cognitive and motor actions. While it is unclear if these temporal connections serve as a DMN subsystem for memory that integrates at the posterior PCu or if these connections suggest a functionally segregated network all together, it is clear that the PCu demonstrates a variety of unique short and long-range connections that likely supports its implication in a variety of higher-order functional roles. Further quantitative analyses are necessary in heterogeneous brain samples in order to clarify the clinical significance of precuneus connectivity throughout human cerebrum.

Acknowledgements Data were provided [in part] by the Human Connectome Project, WU-Minn Consortium (Principal Investigators: David Van Essen and Kamil Ugurbil; 1U54MH091657) funded by the 16 NIH Institutes and Centers that support the NIH Blueprint for Neuroscience Research; and by the McDonnell Center for Systems Neuroscience at Washington University.

Author contributions Author contributions included conception and study design (MES, RGB and IMY), data collection or acquisition (RGB, OT and RDF), statistical analysis (OT, RDF and VD), interpretation of results (IMG, JH, and MYB), drafting the manuscript work or revising it critically for important intellectual content (IMY, ND, MES, YL, JH and OT) and approval of final version to be published and agreement to be accountable for the integrity and accuracy of all aspects of the work (All authors).

Funding No funding was provided for this research study.

Declarations

Conflict of interest Dr. Sughrue is the Chief Medical Officer of Omniscient Neurotechnologies. No products directly related to this were discussed in this paper. All other authors have no financial interests or potential conflicts of interest.

Ethical approval The majority of data used was collected by the Human Connectome Project and its de-identified data is accessible in a public database. They followed the appropriate ethics review board standards, and as it is publicly available, its use is internal review board exempt. The use of cadaver dissections was approved by the State Anatomic Board in Oklahoma, United States.

References

- Andersen, R. A., Andersen, K. N., Hwang, E. J., & Hauschild, M. (2014). Optic ataxia: From Balint's syndrome to the parietal reach region. *Neuron*, *81*(5), 967–983. <https://doi.org/10.1016/j.neuron.2014.02.025>.
- Anderson, J. S., Ferguson, M. A., Lopez-Larson, M., & Yurgelun-Todd, D. (2011). Connectivity gradients between the default mode and attention control networks. *Brain Connectivity*, *1*(2), 147–157. <https://doi.org/10.1089/brain.2011.0007>.
- Andrews-Hanna, J. R., Smallwood, J., & Spreng, R. N. (2014). The default network and self-generated thought: Component processes, dynamic control, and clinical relevance. *Annals of the New York Academy of Sciences*, *1316*(1), 29–52. <https://doi.org/10.1111/nyas.12360>.
- Baker, C. M., Burks, J. D., Briggs, R. G., Conner, A. K., Glenn, C. A., Manohar, K., & Sughrue, M. E. (2018). A connectomic atlas of the human cerebrum—chapter 8: The posterior cingulate cortex medial parietal lobe and parieto-occipital sulcus. *Oper Neurosurg (Hagerstown)*, *15*, S350–s371.
- Briggs, R. G., Allan, P. G., Poologaindran, A., Dadario, N. B., Young, I. M., Ahsan, S. A., & Sughrue, M. E. (2021). The frontal aslant tract and supplementary motor area syndrome: Moving towards a connectomic initiation axis. *Cancers*. <https://doi.org/10.3390/cancers13051116>.
- Briggs, R. G., Chakraborty, A. R., Anderson, C. D., Abraham, C. J., Palejwala, A. H., Conner, A. K., & Sughrue, M. E. (2019). Anatomy and white matter connections of the inferior frontal gyrus. *Clinical Anatomy*, *32*(4), 546–556. <https://doi.org/10.1002/ca.23349>.
- Brodt, S., Pohlchen, D., Flanagan, V. L., Glasauer, S., Gais, S., & Schonauer, M. (2016). Rapid and independent memory formation in the parietal cortex. *Proceedings of the National Academy of Sciences USA*, *113*(46), 13251–13256. <https://doi.org/10.1073/pnas.1605719113>.
- Bubb, E. J., Metzler-Baddeley, C., & Aggleton, J. P. (2018). The cingulum bundle: Anatomy, function, and dysfunction. *Neuroscience & Biobehavioral Reviews*, *92*, 104–127. <https://doi.org/10.1016/j.neubiorev.2018.05.008>.
- Buckner, R. L., Andrews-Hanna, J. R., & Schacter, D. L. (2008). The brain's default network: Anatomy, function, and relevance to disease. *Annals of the New York Academy of Sciences*, *1124*, 1–38. <https://doi.org/10.1196/annals.1440.011>.
- Burks, J. D., Boettcher, L. B., Conner, A. K., Glenn, C. A., Bonney, P. A., Baker, C. M., & Sughrue, M. E. (2017a). White matter connections of the inferior parietal lobule: A study of surgical anatomy. *Brain and Behavior: A Cognitive Neuroscience Perspective*, *7*(4), e00640. <https://doi.org/10.1002/brb3.640>.
- Burks, J. D., Bonney, P. A., Conner, A. K., Glenn, C. A., Briggs, R. G., Battiste, J. D., & Sughrue, M. E. (2017b). A method for safely resecting anterior butterfly gliomas: The surgical anatomy of the default mode network and the relevance of its preservation. *Journal of Neurosurgery*, *126*(6), 1795–1811. <https://doi.org/10.3171/2016.5.Jns153006>.
- Burks, J. D., Conner, A. K., Bonney, P. A., Glenn, C. A., Baker, C. M., Boettcher, L. B., & Sughrue, M. E. (2018). Anatomy and white matter connections of the orbitofrontal gyrus. *Journal of Neurosurgery*, *128*(6), 1865–1872. <https://doi.org/10.3171/2017.3.Jns162070>.
- Caspers, S., & Zilles, K. (2018). Microarchitecture and connectivity of the parietal lobe. *Handbook of Clinical Neurology*, *151*, 53–72. <https://doi.org/10.1016/b978-0-444-63622-5.00003-6>.
- Catani, M., Dell'Acqua, F., Vergani, F., Malik, F., Hodge, H., Roy, P., & Thiebaut de Schotten, M. (2012). Short frontal lobe connections of the human brain. *Cortex*, *48*(2), 273–291. <https://doi.org/10.1016/j.cortex.2011.12.001>.
- Cavanna, A. E. (2007). The precuneus and consciousness. *CNS Spectrums*, *12*(7), 545–552. <https://doi.org/10.1017/S1092852900021295>.
- Cavanna, A. E., & Trimble, M. R. (2006). The precuneus: A review of its functional anatomy and behavioural correlates. *Brain*, *129*(3), 564–583. <https://doi.org/10.1093/brain/awl004>.
- Che, X., Zhang, Q., Zhao, J., Wei, D., Li, B., Guo, Y., & Liu, Y. (2014). Synchronous activation within the default mode network correlates with perceived social support. *Neuropsychologia*, *63*, 26–33. <https://doi.org/10.1016/j.neuropsychologia.2014.07.035>.
- Cheng, W., Rolls, E. T., Qiu, J., Yang, D., Ruan, H., Wei, D., & Feng, J. (2018). Functional connectivity of the precuneus in unmedicated patients with depression. *Biological Psychiatry. Cognitive Neuroscience and Neuroimaging*, *3*(12), 1040–1049. <https://doi.org/10.1016/j.bpsc.2018.07.008>.
- Cunningham, S. I., Tomasi, D., & Volkow, N. D. (2017). Structural and functional connectivity of the precuneus and thalamus to the default mode network. *Human Brain Mapping*, *38*(2), 938–956. <https://doi.org/10.1002/hbm.23429>.
- Dalboni da Rocha, J. L., Bramati, I., Coutinho, G., Tovar Moll, F., & Sitaram, R. (2020). Fractional anisotropy changes in parahippocampal cingulum due to alzheimer's disease. *Scientific Reports*, *10*(1), 2660. <https://doi.org/10.1038/s41598-020-59327-2>.
- De Witt Hamer, P. C., Moritz-Gasser, S., Gatignol, P., & Duffau, H. (2011). Is the human left middle longitudinal fascicle essential for language? A brain electrostimulation study. *Human Brain Mapping*, *32*(6), 962–973. <https://doi.org/10.1002/hbm.21082>.
- Ferri, J., Schmidt, J., Hajcak, G., & Canli, T. (2016). Emotion regulation and amygdala-precuneus connectivity: Focusing on attentional deployment. *Cognitive, Affective, & Behavioral Neuroscience*, *16*(6), 991–1002. <https://doi.org/10.3758/s13415-016-0447-y>.
- Filimon, F., Nelson, J. D., Huang, R.-S., & Sereno, M. I. (2009). Multiple parietal reach regions in humans: Cortical representations for visual and proprioceptive feedback during on-line reaching. *The*

- Journal of Neuroscience*, 29(9), 2961. <https://doi.org/10.1523/JNEUROSCI.3211-08.2009>.
- Finn, E. S., Shen, X., Scheinost, D., Rosenberg, M. D., Huang, J., Chun, M. M., & Constable, R. T. (2015). Functional connectome fingerprinting: Identifying individuals using patterns of brain connectivity. *Nature Neuroscience*, 1, 1664–1671.
- Gertz, H., & Fiehler, K. (2015). Human posterior parietal cortex encodes the movement goal in a pro-/anti-reach task. *Journal of Neurophysiology*, 114(1), 170–183. <https://doi.org/10.1152/jn.01039.2014>.
- Gilmore, A. W., Nelson, S. M., & McDermott, K. B. (2015). A parietal memory network revealed by multiple MRI methods. *Trends in Cognitive Sciences*, 19(9), 534–543. <https://doi.org/10.1016/j.tics.2015.07.004>.
- Glasser, M. F., Coalson, T. S., Robinson, E. C., Hacker, C. D., Harwell, J., Yacoub, E., & Van Essen, D. C. (2016). A multi-modal parcellation of human cerebral cortex. *Nature*, 536(7615), 171–178. <https://doi.org/10.1038/nature18933>.
- Greicius, M. D., Krasnow, B., Reiss, A. L., & Menon, V. (2003). Functional connectivity in the resting brain: A network analysis of the default mode hypothesis. *Proceedings of the National Academy of Sciences U S A*, 100(1), 253–258. <https://doi.org/10.1073/pnas.0135058100>.
- Gürer, B., Bozkurt, M., Neves, G., Cikla, U., Hananya, T., Antar, V., & Başkaya, M. K. (2013). The subparietal and parietooccipital sulci: An anatomical study. *Clinical Anatomy*, 26(6), 667–674. <https://doi.org/10.1002/ca.22277>.
- Harroud, A., Boucher, O., Tran, T. P. Y., Harris, L., Hall, J., Dubeau, F., & Nguyen, D. K. (2017). Precuneal epilepsy: Clinical features and surgical outcome. *Epilepsy & Behavior*, 73, 77–82. <https://doi.org/10.1016/j.yebeh.2017.05.018>.
- He, B., Perez, S. E., Lee, S. H., Ginsberg, S. D., Malek-Ahmadi, M., & Mufson, E. J. (2020). Expression profiling of precuneus layer III cathepsin D-immunopositive pyramidal neurons in mild cognitive impairment and alzheimer's disease: Evidence for neuronal signaling vulnerability. *The Journal of Comparative Neurology*. <https://doi.org/10.1002/cne.24929>.
- Hescher, M., Ibrahim, C., & Gilboa, A. (2020). Precuneus stimulation alters the neural dynamics of autobiographical memory retrieval. *NeuroImage*, 210, 116575. <https://doi.org/10.1016/j.neuroimage.2020.116575>.
- Hwang, E. J., Hauschild, M., Wilke, M., & Andersen, R. A. (2012). Inactivation of the parietal reach region causes optic ataxia, impairing reaches but not saccades. *Neuron*, 76(5), 1021–1029. <https://doi.org/10.1016/j.neuron.2012.10.030>.
- Kalyvas, A., Koutsarnakis, C., Komaitis, S., Karavasilis, E., Christidi, F., Skandalakis, G. P., & Stranjalis, G. (2020). Mapping the human middle longitudinal fasciculus through a focused anatomic-imaging study: Shifting the paradigm of its segmentation and connectivity pattern. *Brain Structure and Function*, 225(1), 85–119. <https://doi.org/10.1007/s00429-019-01987-6>.
- Kamali, A., Sair, H. I., Radmanesh, A., & Hasan, K. M. (2014). Decoding the superior parietal lobule connections of the superior longitudinal fasciculus/arcuate fasciculus in the human brain. *Neuroscience*, 277, 577–583. <https://doi.org/10.1016/j.neuroscience.2014.07.035>.
- Koutsarnakis, C., Liakos, F., Kalyvas, A. V., Sakas, D. E., & Stranjalis, G. (2015). A laboratory manual for stepwise cerebral white matter fiber dissection. *World Neurosurgery*, 84(2), 483–493. <https://doi.org/10.1016/j.wneu.2015.04.018>.
- Kwok, S. C., Shallice, T., & Macaluso, E. (2012). Functional anatomy of temporal organisation and domain-specificity of episodic memory retrieval. *Neuropsychologia*, 50(12), 2943–2955. <https://doi.org/10.1016/j.neuropsychologia.2012.07.025>.
- Leech, R., Kamourieh, S., Beckmann, C. F., & Sharp, D. J. (2011). Fractionating the default mode network: Distinct contributions of the ventral and dorsal posterior cingulate cortex to cognitive control. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, 31(9), 3217–3224. <https://doi.org/10.1523/JNEUROSCI.5626-10.2011>.
- Leichnetz, G. R. (2001). Connections of the medial posterior parietal cortex (area 7m) in the monkey. *Anatomical Record*, 263(2), 215–236. <https://doi.org/10.1002/ar.1082>.
- Lin, Y. H., Dhanaraj, V., Mackenzie, A. E., Young, I. M., Tanglay, O., Briggs, R. G., & Sughrue, M. E. (2021). Anatomy and white matter connections of the parahippocampal gyrus. *World Neurosurgery*, 148, e218–e226. <https://doi.org/10.1016/j.wneu.2020.12.136>.
- Lundstrom, B. N., Ingvar, M., & Petersson, K. M. (2005). The role of precuneus and left inferior frontal cortex during source memory episodic retrieval. *NeuroImage*, 27(4), 824–834. <https://doi.org/10.1016/j.neuroimage.2005.05.008>.
- Mahayana, I. T., Hartono, T. L., Chen, C.-Y., Juan, C.-H., & Mugleton, N. G. (2014). Posterior parietal cortex and visuospatial control in near and far space. *Translational Neuroscience*, 5(4), 269–274. <https://doi.org/10.2478/s13380-014-0229-3>.
- Makris, N., Preti, M. G., Wassermann, D., Rathj, Y., Papadimitriou, G. M., Yergatian, C., & Kubicki, M. (2013). Human middle longitudinal fascicle: Segregation and behavioral-clinical implications of two distinct fiber connections linking temporal pole and superior temporal gyrus with the angular gyrus or superior parietal lobule using multi-tensor tractography. *Brain Imaging and Behavior*, 7(3), 335–352. <https://doi.org/10.1007/s11682-013-9235-2>.
- Martino, J., De Witt Hamer, P. C., Berger, M. S., Lawton, M. T., Arnold, C. M., de Lucas, E. M., & Duffau, H. (2013). Analysis of the subcomponents and cortical terminations of the perisylvian superior longitudinal fasciculus: A fiber dissection and DTI tractography study. *Brain Structure and Function*, 218(1), 105–121. <https://doi.org/10.1007/s00429-012-0386-5>.
- Menjot de Champfleury, N., Lima Maldonado, I., Moritz-Gasser, S., Machi, P., Le Bars, E., Bonafe, A., & Duffau, H. (2013). Middle longitudinal fasciculus delineation within language pathways: A diffusion tensor imaging study in human. *European Journal of Radiology*, 82(1), 151–157. <https://doi.org/10.1016/j.ejrad.2012.05.034>.
- Mito, R., Raffelt, D., Dhollander, T., Vaughan, D. N., Tournier, J. D., Salvado, O., & Connelly, A. (2018). Fibre-specific white matter reductions in alzheimer's disease and mild cognitive impairment. *Brain*, 141(3), 888–902. <https://doi.org/10.1093/brain/awx355>.
- Palejwala, A. H., O'Connor, K. P., Pelargos, P., Briggs, R. G., Milton, C. K., Conner, A. K., & Sughrue, M. E. (2020b). Anatomy and white matter connections of the lateral occipital cortex. *Surgical and Radiologic Anatomy*, 42(3), 315–328. <https://doi.org/10.1007/s00276-019-02371-z>.
- Palejwala, A. H., O'Connor, K. P., Milton, C. K., Anderson, C., Pelargos, P., Briggs, R. G., & Sughrue, M. E. (2020a). Anatomy and white matter connections of the fusiform gyrus. *Scientific Reports*, 10(1), 13489–13489. <https://doi.org/10.1038/s41598-020-70410-6>.
- Pereira-Pedro, A. S., & Bruner, E. (2016). Sulcal pattern, extension, and morphology of the precuneus in adult humans. *Annals of Anatomy - Anatomischer Anzeiger*, 208, 85–93. <https://doi.org/10.1016/j.aanat.2016.05.001>.
- Raichle, M. E., MacLeod, A. M., Snyder, A. Z., Powers, W. J., Gusnard, D. A., & Shulman, G. L. (2001). A default mode of brain function. *Proceedings of the National Academy of Sciences U S A*, 98(2), 676–682. <https://doi.org/10.1073/pnas.98.2.676>.
- Saur, D., Kreher, B. W., Schnell, S., Kümmerer, D., Kellmeyer, P., Vry, M.-S., & Weiller, C. (2008). Ventral and dorsal pathways for language. *Proceedings of the National Academy of Sciences*, 105(46), 18035–18040. <https://doi.org/10.1073/pnas.0805234105>.

- Scheff, S. W., Price, D. A., Schmitt, F. A., Roberts, K. N., Ikonovic, M. D., & Mufson, E. J. (2013). Synapse stability in the precuneus early in the progression of alzheimer's disease. *Journal of Alzheimer's Disease: JAD*, 35(3), 599–609. <https://doi.org/10.3233/JAD-122353>.
- Schott, B. H., Wüstenberg, T., Lücke, E., Pohl, I.-M., Richter, A., Seidenbecher, C. I., & Richardson-Klavehn, A. (2019). Gradual acquisition of visuospatial associative memory representations via the dorsal precuneus. *Human Brain Mapping*, 40(5), 1554–1570. <https://doi.org/10.1002/hbm.24467>.
- Sheets, J. R., Briggs, R. G., Bai, M. Y., Poologaindran, A., Young, I. M., Conner, A. K., & Sughrue, M. E. (2020). Parcellation-based modeling of the dorsal premotor area. *Journal of the Neurological Sciences*, 415, 116907. <https://doi.org/10.1016/j.jns.2020.116907>.
- Skandalakis, G. P., Komaitis, S., Kalyvas, A., Lani, E., Kontrafouris, C., Drosos, E., & Koutsarnakis, C. (2020). Dissecting the default mode network: Direct structural evidence on the morphology and axonal connectivity of the fifth component of the cingulum bundle. *Journal of Neurosurgery*. <https://doi.org/10.3171/2020.2.Jns193177>.
- Sreekumar, V., Nielson, D. M., Smith, T. A., Dennis, S. J., & Sederberg, P. B. (2018). The experience of vivid autobiographical reminiscence is supported by subjective content representations in the precuneus. *Scientific Reports*, 8(1), 14899. <https://doi.org/10.1038/s41598-018-32879-0>.
- Thibes, R. B., Novaes, N. P., Lucato, L. T., Campanholo, K. R., Melo, L. M., Leite, C. C., & Sato, J. R. (2017). Altered functional connectivity between precuneus and motor systems in Parkinson's disease patients. *Brain Connectivity*, 7(10), 643–647. <https://doi.org/10.1089/brain.2017.0534>.
- Thiebaut de Schotten, M., Dell'Acqua, F., Forkel, S. J., Simmons, A., Vergani, F., Murphy, D. G., & Catani, M. (2011). A lateralized brain network for visuospatial attention. *Nature Neuroscience*, 14(10), 1245–1246. <https://doi.org/10.1038/nn.2905>.
- Utevsky, A. V., Smith, D. V., & Huettel, S. A. (2014). Precuneus is a functional core of the default-mode network. *Journal of Neuroscience*, 34(3), 932–940. <https://doi.org/10.1523/jneurosci.4227-13.2014>.
- Vindras, P., Blangero, A., Ota, H., Reilly, K. T., Rossetti, Y., & Pisella, L. (2016). The pointing errors in optic ataxia reveal the role of “peripheral magnification” of the PPC. *Frontiers in Integrative Neuroscience*. <https://doi.org/10.3389/fnint.2016.00027>.
- Wagner, A. D., Shannon, B. J., Kahn, I., & Buckner, R. L. (2005). Parietal lobe contributions to episodic memory retrieval. *Trends in Cognitive Sciences*, 9(9), 445–453. <https://doi.org/10.1016/j.tics.2005.07.001>.
- Wang, J., Becker, B., Wang, L., Li, H., Zhao, X., & Jiang, T. (2019). Corresponding anatomical and coactivation architecture of the human precuneus showing similar connectivity patterns with macaques. *NeuroImage*, 200, 562–574. <https://doi.org/10.1016/j.neuroimage.2019.07.001>.
- Wang, Y., Fernandez-Miranda, J. C., Verstynen, T., Pathak, S., Schneider, W., & Yeh, F. C. (2013). Rethinking the role of the middle longitudinal fascicle in language and auditory pathways. *Cerebral Cortex*, 23(10), 2347–2356. <https://doi.org/10.1093/cercor/bhs225>.
- Wei, S., Chang, M., Zhang, R., Jiang, X., Wang, F., & Tang, Y. (2018). Amygdala functional connectivity in female patients with major depressive disorder with and without suicidal ideation. *Annals of General Psychiatry*, 17, 37–37. <https://doi.org/10.1186/s12991-018-0208-0>.
- Wenderoth, N., Debaere, F., Sunaert, S., & Swinnen, S. P. (2005). The role of anterior cingulate cortex and precuneus in the coordination of motor behaviour. *European Journal of Neuroscience*, 22(1), 235–246. <https://doi.org/10.1111/j.1460-9568.2005.04176.x>.
- Whitlock, J. R. (2017). Posterior parietal cortex. *Current Biology*, 27(14), R691–R695. <https://doi.org/10.1016/j.cub.2017.06.007>.
- Wu, Y., Sun, D., Wang, Y., Wang, Y., & Ou, S. (2016). Segmentation of the cingulum bundle in the human brain: A new perspective based on DSI tractography and fiber dissection study. *Frontiers in Neuroanatomy*. <https://doi.org/10.3389/fnana.2016.00084>.
- Xu, X., Yuan, H., & Lei, X. (2016). Activation and connectivity within the default mode network contribute independently to future-oriented thought. *Scientific Reports*, 6(1), 21001. <https://doi.org/10.1038/srep21001>.
- Yang, Z., Chang, C., Xu, T., Jiang, L., Handwerker, D. A., Castellanos, F. X., & Zuo, X. N. (2014). Connectivity trajectory across lifespan differentiates the precuneus from the default network. *NeuroImage*, 89, 45–56. <https://doi.org/10.1016/j.neuroimage.2013.10.039>.
- Yeh, F.-C., Wedeen, V. J. J., & Tseng, W.-Y.I. (2010). Generalized q-sampling imaging. *IEEE Transactions on Medical Imaging*, 29(9), 1626–1635. <https://doi.org/10.1109/TMI.2010.2045126>.
- Yokoi, T., Watanabe, H., Yamaguchi, H., Bagarinao, E., Masuda, M., Imai, K., & Sobue, G. (2018). Involvement of the precuneus/posterior cingulate cortex is significant for the development of alzheimer's disease: A PET (THK5351, PiB) and resting fMRI study. *Frontiers in Aging Neuroscience*. <https://doi.org/10.3389/fnagi.2018.00304>.
- Zhang, S., & Li, C.-S.R. (2012). Functional connectivity mapping of the human precuneus by resting state fMRI. *NeuroImage*, 59(4), 3548–3562. <https://doi.org/10.1016/j.neuroimage.2011.11.023>.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.