

A Theory of Hemispheric Specialization Based on Cortical Columns

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Hemispheric function specialization and associated neuroanatomical characteristics have been a topic of interest for many years. In this regard, mechanisms of cortical processing and memory storage have proven elusive. The current paper proposes that a model of cortical processing based on the column has the potential for explaining laterality of function and memory. Memory formation is defined as the strengthening of synaptic connections in any given circuit of cortical columns, while forgetting is defined as weakened synaptic connections with failure to activate downstream columns in any given circuit. Following a discussion of the cortical column, it is suggested that speed and quantity of columnar activation can explain laterality findings. However, several additional aspects of columnar interaction patterns must be considered to explain the regional differences within each of the hemispheres. The paper concludes with a discussion of current approaches that offer a means to test the model's validity.

Keywords: laterality, cortical column, memory, dimensional systems model

Cerebral hemispheric asymmetry of function has been the subject of research for many years using a variety of techniques (Hellige, 2002). In addition to gross structural asymmetries (e.g., planum temporale), there are indications of cytoarchitectonic and biochemical differences. However, it has recently been suggested that a more promising way to organize human cortical function is along the lines of dorsal and ventral systems. Borst, Thompson, and Kosslyn, (2011) noted that the two hemispheres seem to have redundant functions,

with most differences appearing to be quantitative (e.g., speed) as opposed to qualitative.

The search for the neural code of processing and memory in the cortex has proven elusive. There has been ongoing debate about just how functionally specialized are the regions of the brain, with disagreement about whether only basic sensory and motor functions are functionally specialized (Kanwisher, 2010). Highlighting such controversy was a recent series of articles in *Psychological Review*. Bowers (2009, 2010) took the position that “grandmother cells” (i.e., localist model) represented a biologically plausible manner of information storage in the cortex, while this was criticized in two other papers (Plaut and McClelland, 2010; Quian Quiroga and Kreiman, 2010) as lacking sufficient explanation as to exactly how the cortex stores such information as opposed to a more distributed pattern.

In a thought provoking article, Gazzaniga (2010) provides insight as to how scientists tend to miss an important concept — the need for the correct level of explanation for understanding the mind. The article’s conclusion is that the brain is a decision-making device and should be understood in those terms. Bassett and Gazzaniga (2011) provided further elaboration on investigating the complexity of the mind/brain interface. In the article, they mentioned the existence of minicolumns and columns, but offered no suggestions on the manner in which these could feasibly interact to create higher cortical functions. One of the questions posed at the conclusion of the article is “What theories need to be developed to guide further research?” (p. 208) The current paper takes the position that the theory needed is one which identifies the manner in which cortical processing occurs and memories are stored. In this case, the correct level of explanation involves identifying the binary unit (bit) and how the interconnection of those units (i.e., the brain) can lead to higher cortical functions (i.e., the mind).

The idea that the cortical column is relevant in the understanding in cortical processing is certainly a controversial issue in its own right. In their review of 50 years of research, Horton and Adams (2005) came “to the disappointing realization that the column may have no function” (p. 837). They reviewed research starting with the 1957 article by Mountcastle who originally hypothesized the column was the “elementary unit organization in the somatic cortex” (p. 430). Although Horton and Adams acknowledge the existence of columns and the numerous models which have emerged based on the concept, they emphasize that no tangible progress has been made. They believe the column has failed to be a unifying principle for the understanding of cortical function. The disappointing aspect is based on the fact that if it were possible to understand one part of the cortex which was representative of the whole, the task of explaining cortical functioning would be simplified immensely. In the closing paragraph, they suggest the column may be a “spandrel” as the term was used by Gould (1997) to describe non-adaptive structures which later in some species become harnessed second-

arily for some purpose. As explained, a spandrel is an architectural term used to describe the remaining triangular space when an arch cuts through the surrounding rectangular framework. Despite being present, spandrels are functionally irrelevant.

In an opposite view, a paper by Moss (2006) proposed the dimensional systems model of cortical organization and function. It was suggested that the cortical column (macrocolumn) is the bit at which all cognitive knowledge is coded. As opposed to suggesting a single dichotomy based on identified functions, several cortical dimensions were proposed based on patterns of columnar interactions. In relation to hemispheric asymmetry, it was suggested that processing speed and the numbers of involved columns from the point of sensory input to the point of behavioral output were responsible, though there were other dimensions within each of the hemispheres. For example, the aforementioned dorsal and ventral systems discussed by Borst et al. (2011) were included in the simultaneous–sequential columnar dimension of the dimensional systems model, though these were viewed as intrahemispheric processing modes used by both the right and left hemispheres.

Over the past six years, there have been a number of studies which would appear to support the cortical aspects of that theory and the current paper will discuss these. There is also a discussion of some revisions and additions to the cortical aspects of the model based on the additional data. Prior to discussing the model in relation to laterality, information on columns is presented.

Cortical Columns

Mountcastle (1957) was the first to describe the existence of cortical columns. Two levels of vertical organization of columns have been identified (Calvin, 1995). These are minicolumns and columns (also referred to as “macrocolumns,” though the current paper will use the term columns). Calvin indicates minicolumns contain between 100 and 200 neurons and have a diameter of about 30 μm . Columns contain at most several hundred minicolumns and have a diameter ranging from 0.4 to 1.0 mm.

In considering the possible level at which the cortical bit might exist, Moss (2006) suggested it could be at the level of the single neuron, minicolumn, or macrocolumn. It was concluded the column would be the best candidate as the basic unit since it would be resistant to damage, and overlapping columns (i.e., sharing neurons within minicolumns) would allow for the large volume of information contained in the cortex. Calvin (1995) discussed the unusual pattern of superficial pyramidal neurons that suggest a columnar organizing principle. The collateral axon travels a characteristic lateral distance without giving off any terminal branches, but then produces a tight terminal cluster. The distance to the center of the terminal cluster is approximately 0.43 mm in the primary visual cortex, 0.65 mm in the secondary visual areas, 0.73 mm in the somatosensory

strip, and 0.85 mm in the motor cortex. It may then continue for an identical distance and produce another cluster, in some cases continuing for several millimeters. This suggests the size of each column is determined by the cluster distances.

Moss (2006) also suggested that the millions of minicolumns were “hard-wired” at birth. The columns of the primary receiving areas would be the first to form based on sensory relay from the thalamo-cortical connections. The primary receiving columns would project outward. The intersection points where axonal terminal bundles of two or more primary receiving columns’ efferent projections meet would become a new column (“information bit”) composed of a similar number of minicolumns. New columns would pass along efferent information in similar fashion with each intersecting bundle of minicolumns forming additional columns.

In an interesting study, Perin, Berger, and Markram (2011) did whole cell recordings of layer 5 pyramidal neurons in rat somatosensory cortical slices. The animals were 14 to 16 days postnatal. Perin et al. found synaptic clusters of neurons in which the highest number of connections were separated by a mean distance of 100 to 125 μm , extending beyond individual minicolumns. However, these extended across distances equivalent to the diameter of a functional neocortical column. Thus, cell assemblies are not arranged randomly or in a lattice, but as small world networks without hubs. Perin et al. noted that the findings are inconsistent with a “clean slate” on which any configuration could be molded. They believed the results suggested that experience could mold overall neuronal circuitry by combining elementary assemblies. Moreover, they believed this could allow for vast memory storage capacity, but also ensure the stability of memories in the face of ongoing activity.

These results provide support for two aspects of the dimensional systems model and add another very interesting possibility. The hardwiring at birth of connections at distances 100 to 125 μm (i.e., corresponding to the size of minicolumns) is consistent with the suggestion of Moss (2006). Additionally, the columnar-sized diameter that these extend is consistent with a column being the level of the information bit. However, the fact that all the neighboring cells within a minicolumn do not project as a unitary cell assembly may indicate that not only do columns overlap and share neurons, so also do minicolumns.

Hebb’s (1949) postulate was originally formulated as an explanation for the cellular basis of learning and memory. The hypothesis was that the coordinated activity of pre- and post-synaptic membranes strengthens the connection between them. Moss (2006) proposed that memory could be defined based on columnar connections. A formal definition of memory formation is the strengthening of synaptic connections in any given circuit of cortical columns. The strengthening occurs due to ongoing reactivation of the circuit with resultant increased probability of downstream synaptic activation initially being the result of neurochemical factors (e.g., ionic concentrations, neurotransmitter stores), followed

by gradual synaptic structural growth (increased axonal boutons and dendritic spines). Forgetting is the result of weakened synaptic connections with failure to activate downstream columns in any given circuit. In this case, the probability of a column's activation by one or more other columns fails to be maintained. However, with structural changes such as axonal sprouting and increased dendritic spines between neurons of columns, then the likelihood of "forgetting" is greatly reduced.

Columnar organization occurs in the somatosensory, auditory, and visual primary receiving areas of the cortex (Cechetto and Topolovec, 2002). There are also columnar aggregates in the human motor cortex (Mountcastle, 1997). In monkeys, there have been studies showing columnar organization in the inferior temporal cortex (Fujita, Tanaka, Ito, and Cheng, 1992; Kreiman, Hung, Kraskov, Quian Quiroga, Poggio, and DiCarlo, 2006; Sato, Uchida, and Tanifuji, 2009; Tamura, Kaneko, and Fujita, 2005; Tanaka, 2000; Tsunoda, Yamane, Nishizaki, and Tanifuji, 2001) and the dorsolateral prefrontal cortex (Hirata and Sawaguchi, 2008). Thus, there is sufficient evidence that a columnar organizational pattern exists in non-human cortex. In reference to human cortex, recent refinement in fMRI methods have allowed identification of columns for ocular dominance (Yacoub, Shmuel, Logothetis, and Ugurbil, 2007), temporal frequency (Sun et al., 2007), and orientation (Yacoub, Harel, and Ugurbil, 2008), in V1, as well as motion columns in MT (Zimmerman et al., 2011).

Three studies are of particular interest in relation to the overlapping columnar arrangement suggested by Moss (2006). Wang, Tanaka, and Tanifuji (1996) were the first to report findings consistent with overlapping columns tied to object recognition in inferior temporal cortex. Tanaka (2000) provided further support that area TE appeared to use columns as an organizational structure and the columns partially overlap. Using optical imaging *in vitro*, Hirata and Sawaguchi (2008) noted functional columns in the dorsolateral prefrontal cortex of the macaque. The columnar activity was evoked by stimulating the middle layer of the prefrontal cortex. The activity did not spread horizontally beyond a certain width, even in the presence of strong electrical stimulation. Hirata and Sawaguchi cite their own and others' research indicating that GABAergic inhibition limits the horizontal spread of activity, and lateral inhibition by GABAergic interneurons may work between neighboring functional columns. Finally, they showed that different columnar activities with only slight overlaps were induced by stimulation at different sites in the same slice. Thus, the existence of overlapping columns with surround inhibition has been supported.

Columnar surround inhibition may provide insight into the recent findings of Linke, Vicente-Grabovetsky, and Cusak (2011). In a functional magnetic resonance imaging study, 20 subjects performed a simple change detection task. Multivoxel pattern analysis of the auditory cortex and Heschl's Gyrus demonstrated robust frequency-specific activations during the encoding phase. This

was consistent with the expected tonotopic organization. In contrast, these areas showed frequency-specific suppression during the maintenance period. Linke et al. proposed that such suppression in the early sensory regions may act as a natural gate-keeping mechanism to prevent irrelevant stimuli from overwriting the information currently stored.

The dimensional systems model explanation of these findings is that the primary receiving columns are activated in a frequency-specific manner. As the information stream proceeds, the higher order columns are activated. However, these columns have a strong surround inhibition. As noted by Moss (2006), "The inhibitory fields around the columns of the new memory would strengthen (i.e., signal) the new columnar array since all but the immediately adjacent or overlapping columns (i.e., noise) are being activated in that region" (p. 235). Thus, only the columns tied to the memory would be active with a pronounced inhibition, or suppression, of the adjacent areas around those columns. Consistent with this interpretation, Linke et al. (2011) stated, "One possibility, given that high-resolution scanning sequences still sample voxels containing many neurons, is that the neurons tuned to the information held in memory still fire during maintenance, whereas closely surrounding, differently tuned neurons are suppressed" (p. 12964).

Using a dynamic computational model, Lucke (2009) evaluated receptive field self-organization possibilities in V1 cortical columns. Based on the fine-scale structure of columns, the model involved subpopulations of excitatory neurons and their interaction with systems of inhibitory neurons. The model gave rise to specific types of computations that result in self-organization of afferents to the column. It was found that for a given type of input, self-organization reliably extracts the basic input components represented by neuronal receptive fields. It was noted that such self-organizing columns' receptive fields were superior to other algorithms, including independent component analysis and sparse coding.

The foregoing discussion would appear to support the contention that a columnar organization pattern exists. In relation to dynamic formation of columns, a study by Muir and Douglas (2011) is relevant. They note that the cortex shows surprising regularity in its repeated motifs of network design. The "superficial patch system," or "daisy architecture," is one such motif described in mapping connections of cortical tissue by the injection of the neuronal tracer horseradish peroxidase (i.e., an enzyme allowing the visualization from the axon terminal to the cell body). Originally described by Rockland and Lund (1982), the motif refers to a series of bands or patches of dense label from the injection site, separated by regions of weak label. Muir and Douglas (2011) note this pattern has been demonstrated across cortical regions of various species. They contend that such universality may indicate this system "can be adapted to many tasks and forms part of the fundamental substrate for cortical

computation” (p. 1118). They note there is a common assumption that labeled patches are composed of clustered axonal projections arising from the pyramidal cells of superficial layers, spreading for several millimeters within a cortical area.

Testing several geometric organizational rules, Muir and Douglas (2011) felt the best fit was one that used information distributed across the cortical sheet to generate axonal projections. They concluded that single neuron information cannot account for such a system, and that information shared across the population of patch-projecting neurons is required. Moreover, the evidence of preferential projections within a cortical area for regions of similar function would be consistent with functional units defined by static neural connectivity. One possible manner in which they believed the patch system could develop across the cortex is by neural activity. Such an explanation is consistent with the dynamic column formation pattern proposed in the dimensional systems model. It is also in line with a study on the horseradish peroxidase in the cat visual cortex by Alekseenko, Toporova, and Makarov (2005). These authors concluded that the initial stages of visual space representation in the cortex can be identified on the basis of data on the topography of direct connections between individual columns in fields 17, 18, 19, and 21a.

Jones and Rakic (2010) posit that columnar-based input may lead to columnar-based output although this has not received much consideration in the past. One article has provided evidence of such dynamic column formation in cortical development: Kaschube, Schnabel, Wolf, and Lowel (2009) showed that columnar architectures of different areas of cat visual cortex develop in a coordinated manner. Orientation columns were analyzed during the critical development period of six to 15 weeks in areas V1 and V2 in both hemispheres. The results were consistent with column-size matching of V1 and V2 both within and between hemispheres, with progressive improvement during the late phase of the critical period. They hypothesized that the emergence of column-size matching is brought about by activity-dependent interactions mediated by interareal connections. Kaschube et al. ended the article with the following comment which is consistent with the dimensional systems model: “Because cortical processing in general takes place in networks distributed across many areas, it is conceivable that a progressive matching of local circuits serving different submodalities is a general characteristic of cortical network formation” (p. 17209).

One last point tied to the column involves cortical layers. Moss (2006) suggested that all layers are involved within the column. Layer 2 was discussed as potentially having inhibitory vertical control over neurons in other layers. Brown et al. (2011) found that neocortical inhibitory interneurons were produced as spatially organized clonal units which were not randomly dispersed. Instead, the inhibitory interneurons formed spatially isolated clusters in the neocortex with clear vertical and horizontal organization. Similarly, Meyer et al. (2011)

found that inhibitory interneuron distribution within columns indicate a cylindrical outline of a cortical column in supragranular layers. This led to the conclusion that cortical columns are relevant functional units beyond input layer 4.

In conflict with the predominant dichotomous view of explicit versus implicit memory, Moss (2006) proposed that all cortical memories are the result of the same basic rules of columnar interactions. In this regard it is suggested that similar neurochemical and neurostructural changes of cortical columns explain all memories. A similar proposal was supported by a recent paper by Reder, Park, and Kieffaber (2009). They provided a thoughtful review and critique of the literature with the proposition that explicit and implicit memories are not a function of separate systems. Reder et al. employed the generic term “node” assuming a localist (as opposed to a distributed) memory representation that is connected to other nodes. Using a computational model called source of activation confusion, they explained how this supports their view that implicit and explicit memory utilize the same memory representations, or nodes. Obviously, the thesis of the current paper is that the column is in fact the cortical node.

One other aspect of the dimensional systems model is that the columns involved in original processing are the same as those involved with the actual memory. In a recent article, Nosofsky, Little, and James (2012) noted that some models of cognition view perceptual categorization and recognition as recruiting the same memory system, while the prevailing view in cognitive neuroscience appears to be that separate neural systems mediate these processes. Employing fMRI and controlling for stimulus and parameter-related differences, they found little indication that categorization and recognition recruit different memory systems.

To understand how the same columnar processes occur in what would appear to be very different forms of processing and memory, Moss (2006) proposed several ways (called dimensions) that cortical columns can be arranged. These were: unorganized–organized; simultaneous–sequential; sensory–nonsensory; and analytical–global. Additionally, two types of cortical memory storage were discussed, one being factual–generic and the other personal–episodic. Following a discussion of the unorganized–organized dimension, the lateralization dimension of analytical–global will be presented. The other dimensions will then be discussed within the lateralization domain. Only a brief description of each dimension will be presented since the full explanation of each was provided in the original article.

Unorganized–Organized

The dimension of unorganized–organized will always be present in the processing of sensory information at the cortical level. In this case, columns representing more basic, or lower-order, information interconnect to higher-order (more-organized) columns. This is along the lines of an “AND-gate” in which two or

more lower-order columns lead to the activation of a single higher-order column. When this occurs, the single higher-order column now represents all the information of its lower-order inputs in a feed-forward manner. It appears that such gating mechanisms are likely seen at all levels of the nervous system since simple logic operations such as OR-gates and AND–NOT-gates have computationally been shown in the spines of dendrites (Shepherd, 2008).

Moss (2006) used the example of language development to explain this concept. In brief, columns which represent specific component phonemes activate when a spoken word is heard and these, in turn, activate the word column. The sequential pattern required for phoneme columns to activate the new location of a word column is determined spatially. Since the axonal projections of all phoneme columns that form a word are activated in a specific order, the first activated will have its efferent activity travel further than the next one activated. The spatial location of the new word column will be determined by the efferent travel distance associated with the location where the two or more phoneme column terminal branches meet. Importantly, if the phonemes of the newly formed word column are presented in a different sequence, the word column is not activated. This is due to the different sequence resulting in a different spatial location of the column being activated. Biederman (1987) noted there are 44 phonemes which compose the English language, which certainly appears to make the foregoing hypothesis feasible since only 44 columns would be necessary. However, this does not exclude the possibility of additional forms of basic speech units (e.g., syllables) being stored at the cortical level as well, which have the capacity to activate purported word columns.

The foregoing description appears compatible with Nourski and Brugge's (2011) discussion of temporal sound features in the human auditory cortex. The core auditory cortex is composed of a primary field and one or more primary-like fields which receive direct input from the ventral medial geniculate nucleus of the thalamus. The core region is surrounded by as many as seven to eight fields comprising the belt region, receiving input from the dorsal medial geniculate nucleus and adjacent core areas. Studies suggest the core region can maintain robust explicit temporal representation of repetitive stimuli up to 200 Hz and beyond which encompasses adult male and female voices. The posterolateral superior temporal region tends to have a considerably lower phase locking capacity suggesting that at higher modulation frequencies, temporal information is transformed into different representations based on discharge rate, or cortical place, or both. The authors note this transformation would be consistent with a hierarchical core belt to parabelt serial or parallel processing model of primate auditory cortex.

There have been recent results indicating hierarchical organization for intelligent speech (Okada et al., 2010). Using fMRI, results consistent with core auditory low-level feature coding which are then combined at higher levels in

the auditory system for greater abstraction were obtained. In this regard, core auditory regions exhibited high levels of sensitivity to acoustic features, while downstream auditory regions in the anterior and posterior superior temporal sulcus bilaterally showed greater sensitivity to speech intelligibility and less sensitivity to acoustic variation (acoustic invariance). Since acoustic invariance was most pronounced in more posterior regions of both hemispheres, the authors believed this supported phonological level representations.

An anterior superior temporal response pattern consistent with hierarchical arrangement was also reported in relation to other aspects of acoustic features of auditory objects (Leaver and Rauschecker, 2010). As with the Okada et al. (2010) study, Leaver and Rauschecker identified regions along the superior temporal plane closer to the primary auditory cortex were not sensitive to stimulus category, responding to specific acoustic features embedded in natural sounds. They found single phonemes or two-phoneme strings activated the left middle superior temporal sulcus to be optimally sensitive to human speech, with the authors suggesting this is a sub-region for acoustic-phonetic speech and not semantic or lexical content. The right anterior superior temporal plane responded preferentially to musical instrument sounds.

In addition to auditory stimuli, all other sensory processing of columnar information is purported to move from less-organized to more-organized. In relation to somatosensory processing, Reed et al. (2008) examined the interaction of neurons of anesthetized owl monkeys at different hand locations. The results indicated spike timing correlations between neurons separated by millimeters of cortex, extending beyond the representation of the palm pad location. This was felt to reflect functional connectivity. They postulated:

Synchrony in unconscious animals implies specific anatomical connectivity between neurons, and population of neurons, and emphasizes that higher levels of integration must consider low-level integration We propose that neurons, even at the first level of somatosensory cortex, participate in global aspects of stimulus processing, on which higher-level processing is based. (p. 10236)

Similarly, there is evidence that visual processing of faces is hierarchically arranged. In relation to four of the six interconnected face-selective regions of the macaque monkey, Freiwald and Tsao (2010) found that neurons in two middle patches were view specific. In the anterior lateral patch, neurons were tuned to identify mirror-symmetrically across views, achieving partial view invariance. Neurons in anterior medial, the most anterior patch, achieved almost full view invariance. This was consistent with results of Tsunoda et al. (2001) in which an object is represented by the combined activation of columns, each responding to a specific visual feature of an object.

In the human visual cortex, Kubilius, Wagemans, and Op de Beeck (2011) employed fMRI to study the behavioral configural-superiority effect. This effect

refers to the fact that a visual search for an odd element is more efficient when that element is part of a configuration as opposed to being presented in isolation. They found evidence supporting a feed-forward cortical shape processing hierarchy in a bottom-up fashion which is consistent with the unorganized-organized dimension of the dimensional systems model. In the same manner that only a very limited number of phonemes are involved in language, Biederman (1987) suggested that there are about 36 basic elements which can be combined to form any complex design. Again, this means only a few lower-order columns would be required to allow more complex configurations in the higher-order columns.

In relation to motor output, the information moves from more-organized to less-organized in relation to the columns. Therefore, one higher-order cortical column activates more numerous lower-order columns. This allows a planned movement represented by a single column to occur since multiple primary motor columns are required to accomplish the movement. The non-motor columns of the frontal lobe would be expected to follow the same higher-order to lower-order principle.

In a study supporting a hierarchical organization of the prefrontal cortex along a rostro-caudal axis, Badre and D'Esposito (2007) conducted four mini-experiments across two fMRI sessions. Each mini-experiment varied competition at one of four hierarchical levels of representation (i.e., manual responses, feature-to-response mappings, perceptual dimensions that comprise a set of relevant perceptual features, and contextual cue-to-dimension mappings). Results indicated that dorsal premotor cortex is sensitive to response competition, anterior dorsal premotor cortex is sensitive to feature competition, inferior frontal sulcus is sensitive to dimension competition, and frontal polar cortex is sensitive to context competition. The authors concluded that the results provide strong support for cognitive control being organized in a rostro-caudal representational hierarchy.

Global-Analytical

The lateralized dimension of the cortical system is global-analytical. The distinction between these types of processing can be understood at two levels: the area containing the information units (i.e., cortical columns) and the total number of available units in any given circuit that can be processed. In contrasting the two processing types, global processing would utilize fewer total columns between stimulus input and the associated response than would analytical processing.

An indication of greater interconnectivity would be increased white matter consistent with myelination. Penhune, Zatorre, MacDonald, and Evans (1996) employed MRI to demonstrate that in the region of the primary auditory cortex of the human brain there is greater white but not gray matter in the left hemisphere. Using histological data from 21 postmortem human cases, Harasty,

Seldon, Chan, Halliday, and Harding (2003) found that the volumes of the left and right planum temporale were approximately equal. However, the left planum temporale was long and thin with the corresponding right area being short and thick. Based on previous studies in the context of their findings, the authors felt the left cortical region was stretched by greater white matter growth which would result in greater distances between columns.

Another histological study of the temporal lobes involved Brodmann area 22 of seven postmortem subjects (Galuske, Schlote, Bratzke, and Singer, 2000). Neuronal tract tracing revealed a modular pattern of connections linking regularly spaced clusters of neurons. The authors believed the clustering was consistent with interdigitating subsystems of selectively interconnected columns. Cluster sizes were similar in both hemispheres, though there was a wider spacing between clusters on the left. This was interpreted as allowing more subsystems existing per surface unit in the left than the right area 22. Calculations based on the measured cluster size and spacing suggested the left can contain about 30% more distinct subsystems within the same volume of tissue.

In their review on hemispheric asymmetries, Hutsler and Galuske (2003) cite their own (e.g., Hutsler, 2003) and others' studies demonstrating significantly larger spacing between interconnected clusters of neurons on the left, though having the same size on both sides. The data indicate there are a greater number of selectively interconnected columns in the left hemisphere. Hutsler and Galuske believe an attractive hypothesis is that structural asymmetries guide functional asymmetries. In this regard, they state that genetically or early ontogenetic events may lead to a structural minicolumn asymmetry which guides functional lateralization. The lateralization might then shape columns to optimize them for language relevant processing.

More recent studies have supported the existence of structural asymmetries. Using diffusion-weighted MRI, Iturria-Medina et al. (2011) investigated whether both hemispheres demonstrate dissimilar general structural attributes that imply different principles on organization of the information flow in human and nonhuman primates. The results showed that the left hemisphere had more central or indispensable regions for the whole-brain structural network than the right hemisphere. It was also found that the right hemisphere is significantly more efficient and interconnected than the left hemisphere. Since the findings were true of both the human dataset and the single macaque dataset, the authors suggested this may indicate a general organizational strategy which is broadly similar between the species. In terms of functional principles, Iturria-Medina et al. believed the results supported two facts: the left hemisphere has a leading role for highly demanding specific processes requiring dedicated specialized networks, while the right hemisphere has a leading role for more general processes requiring a relatively greater general level of interconnectivity.

Kang, Herron, and Woods (2011) used diffusion tensor imaging and magnetization transfer imaging measurements of pericortical white matter tissue and observed greater fiber coherence and increased myelination of fibers in left hemispheric regions. Highly consistent hemispheric asymmetries in fractional anisotropy and magnetic transfer ratio were observed. The authors suggested that the greater fiber coherence and increased myelination of fibers in left hemisphere perisylvian regions may provide a structural basis for left-hemisphere language dominance.

Using MRI gray matter R1 mapping, which is a property related to myelin content, Sigalovsky, Fischl, and Melcher (2006) found indications of greater gray matter myelination in left compared to right auditory cortex in living humans. The areas assessed included Heschl's gyrus, planum temporale, superior temporal gyrus, and superior temporal sulcus. This was interpreted as being consistent with the left hemisphere being preferentially involved in the processing of rapid temporal changes in acoustic signals, including speech.

In an assessment of music processing, Perani et al. (2010) assessed one- to two-day-old newborns using fMRI while the infants heard music and altered versions of the same excerpts. When music was played, right-hemispheric activation was seen in both the primary and higher-order auditory cortex. When the music was altered, the activation reduced in the right auditory cortex, and emerged in the left inferior frontal cortex and limbic structures. The results were considered to demonstrate that the infant brain has hemispheric specialization in processing music as early as the first postnatal hours. Perani et al. believed results also indicated the neural architecture for music processing is sensitive to changes in tonal key. Overall, they noted the hierarchical organization of music processing very early in life is complementary to previous research which supported an interpretation of complex hierarchical organization of auditory language in infants.

Morillon et al. (2010) provided data that supported intrinsic lateralized language network activity as a result of human cerebral asymmetry for language. They found that in the absence of language-related processing, left auditory, somatosensory, articulatory motor, and inferior parietal cortices show specific, lateralized, speech-related physiological properties. Morillon et al. believed the results support theories for intrinsic, hardwired perceptual motor processing in syllabic parsing. Specifically, they concluded there appears to be an inherent auditory-motor tuning at the syllabic rate, as well as an acquired tuning at the phonemic rate which would be consistent with two recognized stages of language development in infants.

The parallel processing view of the hemispheres of the dimensional systems model has also led to the proposition that the hemisphere arriving at a solution the fastest is the one which controls the ensuing response (Moss, 2006). Ratinckx

and Fias (2007) investigated processing speed in a number comparison study. They concluded that the results could be interpreted in a simple race model in which two independent and parallel hemispheric processes compete for the control of response. In this case, the faster process wins.

In summary, the foregoing discussion provides support for the column as the basic cortical information bit arranged hierarchically within each hemisphere, with the left's analytical processing style resulting from a larger number of interconnected columns which, in turn, results in slower processing speed compared to the right hemisphere. The discussion will now shift to explaining the hypothesized intrahemispheric dimensions.

Simultaneous–Sequential

Simultaneous processing simply means that a number of columns are being activated at the same time. In this manner, more-organized, or higher-order, information depends upon lower-order columns being simultaneously activated. Sequential processing reflects one column being activated at a given time. For a higher-order column to be activated, the inputs from its lower-order columns must be received in a specific temporal pattern. Thus, if the order of stimulus input is altered, even though the same stimulus input occurs, a different higher-order column will be activated.

Moss (2006) proposed that different types of sensory input require different processing patterns. Based on the processing required, the proximal cortical regions perpetuate the same mode of processing. Somatosensory information requires simultaneous processing, while auditory information relies on sequential processing. Vision requires both modes. This organizational pattern would result in the more dorsal cortical regions following a simultaneous pattern, with the more ventral areas following a sequential pattern. The intermediate areas would combine both modes.

When a task involving highly processed information involving one mode of operation also requires the addition of highly processed information from a different mode, the two areas connect directly. For example, visual input involves both simultaneous and sequential information. If the task at hand requires spatial features (requiring all aspects be appreciated at the same time), the processing stream goes toward the parietal area which involves simultaneous processing. On the other hand, if information requires sequential patterning (i.e., only one final aspect be appreciated), it proceeds toward the temporal lobe. These correspond to the “where” and “what” pathways, respectively. If the task requires both processing types, the higher-order (i.e., more highly organized information being represented by that column) columns in the occipito-parietal and posterior temporal regions would interconnect directly with higher-order anterior and inferior temporal columns. The location where this interconnection occurs is

the medial temporal lobe cortex as has been suggested by Diana, Yonelinas, and Ranganath (2007).

Let us assume a task in which a subject is shown a picture of five familiar individuals and then subsequently asked to state from memory where in the picture a particular person was located. This requires the individual to use simultaneous processing (i.e., spatial information) in visualizing the picture. While temporarily “holding” this image, there must be a sequential analysis to locate the specific individual. This would theoretically result in posterior cortical activation in the occipito-parietal (columns associated with visualizing the picture) and anterior–inferior temporal regions (columns associated with the target individual’s identity), in addition to the corresponding frontal columns (ventral columns associated with self-talk of the task directions, dorsolateral columns selecting the individual based on the temporal lobe column identity, and the more dorsal columns activating the occipito-parietal columns related to the spatial visualization).

In situations requiring rapid, ongoing updating of information, processing would occur in convergence zones. For example, area MT involved with motion detection involves both simultaneous (entire visual space) and sequential processing (moving object) in conjunction and columns in this region would allow rapid information updates.

The foregoing discussion highlights another point in relation to the so-called “functionally specialized” regions of the cortex. The dimensional systems model indicates these regions are simply the location of specific columns representing the final (i.e., highest-order) representation of all associated lower-order columns. For instance, a column in inferior temporal cortex representing the face of a particular individual is the last one of a number of lower-order columns starting in V1 and progressing along the cortex. Thus, there is distributed processing along the ventral stream required for each “face” column in inferior temporal cortex.

In relation to the frontal lobes, the processing mode of a posterior cortical column would lead to the same processing mode in the frontal column to which it connects. Thus, the same dorsal (simultaneous processing) and ventral (sequential processing) distinction would occur in the frontal lobe. The intermediate areas would involve both types of processing. If accurate, this would lead to a better understanding of working memory in various tasks, as well as the role of the supplemental motor cortex involvement in sequential motor tasks. In each case, the dorsal simultaneous processing is required to maintain all aspects of the sequential information contained in the ventral columns.

Consistent with dorsally located simultaneous processing, Harrison, Jolicouer, and Marois (2010) found that the intraparietal sulcus was involved only in response to spatial location information in a visual short-term memory task. There was no effect in relation to object identification which the current model would indicate is related to ventrally located sequential processing.

As was previously discussed, the dimensional systems model suggests that when a task involving highly processed information from one mode of operation also requires the addition of highly processed information from a different mode, the two areas connect directly. In support of this contention, Monosov, Sheinberg, and Thompson (2010) collected data from two monkeys performing a covert search task. In this study, the monkey maintained fixation on a central stimulus and, using a lever, reported the identity of the learned target object among distractors. Simultaneous single neuron recordings were taken in the frontal eye fields and inferior temporal cortex. The frontal eye fields are parts of the dorsal frontoparietal attention network and play a role in the visual–spatial selection process. Results showed that neural activity specifying location was evident in frontal eye fields before neural activity specifying target identity in inferior temporal cortex. The authors suggested this implied a functional linkage between the end stages of “where” and “what” visual processing.

Recording from neurons in the dorsal and lateral prefrontal cortex in four rhesus monkeys, Meyer, Qi, Stanford, and Constantinidis (2011) evaluated patterns before and at multiple stages of training on visual working memory tasks. Eye saccades to either a green or a blue choice target were the required responses in a match versus nonmatch task. Two monkeys were trained on a spatial working memory task, while two others were trained in three working memory tasks as follows: spatial working memory, feature working memory, and conjunction of locations and features working memory. Prior to training there were substantial functional differences between the two regions. Dorsal prefrontal cortex was more responsive to visual stimuli and preferentially selective for spatial information. The spatial bias remained higher for the dorsal region after training, though stimulus selectivity generally decreased. Ventral areas were biased toward non-spatial information, although they were more influenced by training in terms of activation and changes in stimulus selectivity. The authors cited the literature demonstrating anatomical connections between posterior parietal to dorsal prefrontal areas 8 and 46, and between inferior temporal cortex and ventral visual stream to areas 12 and 45 of the ventral prefrontal cortex. Meyer et al. believed the results demonstrated functional differences in addition to the anatomical connections between the dorsal and ventral prefrontal regions, though the domain-specific organization is not absolute.

In their review of data on a rostro-caudal hierarchical arrangement in the frontal lobes, Badre and D’Esposito (2009) noted there is support for a distinction between dorsal and ventral rostro-caudal gradients of the frontal lobes, such that each acts as a coherent functional network. They drew the same conclusion in relation to regions of the parietal and lateral temporal cortices. This is consistent with the dimension of simultaneous (dorsal) and sequential (ventral) modes of columnar processing in relation to the previously discussed unorganized–organized dimension.

The dorsal simultaneous and ventral sequential differentiation has also been shown related to language. Saur et al. (2008) conducted two experiments employing fMRI with diffusion tensor imaging. The first involved overt repetition of aurally presented pseudo words as opposed to real words, with the second requiring attentive listening to meaningful speech versus meaningless pseudo speech. The most probable anatomical pathways were identified. Sublexical repetition appears to involve a dorsal pathway connecting the superior temporal lobe and frontal premotor cortices, while higher-level language comprehension involves a ventral pathway connecting the middle temporal lobe and ventrolateral prefrontal cortex. Saur et al. suggested the dorsal route is mainly restricted to sensory-motor mapping of sound to articulation, while the linguistic processing of sound involves the ventral route.

Reception–Action (Formerly Called Sensory–Nonsensory)

The third dimension described by Moss (2006) was that of sensory–nonsensory. Based on the current model, any memory of action involves columns of the frontal lobe. Actions can refer to motor functions, but can also refer to non-sensory columns interacting without motor functions (e.g., working memory, planning, and analysis). Any receptive sensory memories, including those associated with specific actions, would involve columns in the posterior lobes. Since sensory information is integral to the accurate production of many actions, simultaneous activation of columns interconnecting posterior and frontal cortex would commonly occur. The columns involved in the original processing of information are the same columns involved in the memory storage.

Consistent with the current model, there appears to be some consensus that long-term sensory memories are stored in the relevant cortical regions subserving the given modalities (Doron and Rosenblum, 2010). Baumann, Endestad, Magnussen, and Greenlee (2008) provided support for a model of perceptual memory in which both discrimination and retention of basic stimulus dimensions is a function of low-level perceptual memory stores located at an early stage in the visual process. They found activation of low-level visual areas, in the absence of prefrontal and parietal activation, during delayed discrimination of orientation and spatial frequency.

Winkler et al. (2002) used an experimental model of implicit recognition and testing in relation to auditory memory. Event-related brain potentials demonstrated an accurate representation of tone pitch in the auditory cortex after brief presentation. Winkler et al. interpreted their findings as providing a link between short duration buffering and permanent storage of acoustic information.

In a study involving the rat, Doron and Rosenblum (2010) found that GABAergic interneurons are activated in gustatory cortex in correlation with novel taste learning. They interpreted the results as providing evidence for a local cortical

circuit not only during acquisition, but also during off-line processing and consolidation of taste information.

Vaillancourt, Thulborn, and Corcos (2003) conducted a study in which visuo-motor and motor memory processes were separated from only-visual and only-motor activation. Their findings provided evidence of a distributed network across cortical and subcortical regions that were involved in the visuomotor process used during visually guided tasks. In contrast, in the prefrontal cortex alone was there activation of a localized network tied to retrieval of force output (i.e., grip force) from memory during internally guided actions. This is consistent with motor memory being restricted to the frontal lobe.

Three studies have provided evidence that left ventral premotor cortex is involved not only in speech production, but also speech perception. Kotz et al. (2010) used transcranial magnetic stimulation (TMS) and fMRI to show Broca's area plays a significant role in speech perception that is lexically based. Using a different experimental approach, Tremblay and Small (2011) explored the nature of the interface between speech production and perception. They noted two possible explanations have been proposed, one of which is that the motor circuits involved in producing a perceived action are enacting the action without causing movement (covert simulation). The other view is that there is not any involvement of motor representations in perception, or the role is simply supportive and does not use the identical circuits. Kotz et al. found the left ventral premotor cortex was significantly active in speech perception as it was in production, supporting the covert simulation hypothesis.

Menenti, Gierhan, Segaert, and Hagoort (2011) used fMRI during speech comprehension and production in 24 subjects. Consistent with Tremblay and Small's findings, this study reported cortical areas involved in semantic, lexical, and syntactic processing were basically the same for speaking and for listening. The overlap included auditory cortex and left inferior frontal cortex, with motor cortex being involved only while speaking.

Factual–Generic and Personal–Episodic Memories

One other aspect of the dimensional systems model suggested by Moss (2006) is that there are two different types of memory stores involving distinct cortical areas. Making a distinction between factual–generic and personal–episodic memories has value in a clinical sense, such as explaining “flashbulb memories” in posttraumatic stress disorder (Moss, 2007). However, during the process of the current review, such a distinction obscures an important point. Based on the purported columnar processing model, memory is simply the columns involved in the original processing of stimuli. As a result, it seems more reasonable to define the memory on the basis of those columns involved. Therefore, episodic memory would refer to sequential processing since this would

be necessary for any temporal information. As discussed below, personal memory would refer to the columns involved medially and close in proximity to the somatosensory area. Generic memories would involve more simultaneous processing and columns in the posterior cortex reflecting less-organized information.

As a case in point, Sajonz et al. (2010) provided evidence that self-referential processing can be distinguished from episodic memory. In an fMRI study involving the use of pictorial stimuli, self-relatedness and episodic aspects were varied. Self-referential processing was found to activate the posterior cingulate–anterior precuneus, medial prefrontal cortex, and an inferior portion of the parietal lobe. Episodic memory involved the posterior precuneus, right anterior prefrontal cortex, and a superior portion of the inferior parietal lobe. Common to both were activations in the intermediate regions within the precuneus and inferior parietal lobe.

In another study which demonstrated the distributed nature of various aspects of autobiographical memory, Daselaar et al. (2008) evaluated a time course across brain regions utilizing fMRI. Subjects signaled during recall of personal memories in response to auditory word cues. Initial versus late period aspects were differentiated. In relation to accessing and maintaining memory, the initial period involved hippocampal, retrosplenial, medial prefrontal, and right prefrontal activity, while the later period activated visual, precuneus, and left frontal activity. Emotional intensity ratings were associated with amygdala and hippocampus activity. The reliving ratings had associated activity in visual cortex, as well as ventromedial inferior prefrontal regions during the later periods. Frontopolar cortex activity was associated with emotional intensity across both periods.

It was proposed by Moss (2006) that thalamic association nuclei interconnected with association cortex provided the means to allow maintenance of activation in the columns of the association cortex. This in turn leads to enhanced synaptic connectivity between the involved columns and memory formation. Enhanced arousal was suggested to increase memory consolidation via increased excitation of the thalamo-cortical circuits. This purported thalamo-cortical circuit leading to strengthening of columnar connections (i.e., memory) may also explain sleep's role in consolidating recently formed memories (Stickgold, 2005). In this case, increased thalamo-cortical activity during sleep would further strengthen the newly formed columnar neuronal connections.

A discussion of the role of the hippocampus in memory was basically omitted in the paper by Moss (2006). When the theory was originally conceived in 1984, it was unclear as to what role the hippocampus and associated medial temporal areas could play in memory storage of cortical columns located at a distance. However, it is now clear that the hippocampus is involved with the storage of new memories.

A theoretical proposal which is consistent with the dimensional systems model is that the hippocampus promotes the process of the gradual integration of newly acquired information into cortical associative networks via binding, reactivating, and strengthening connections (Rasch and Born, 2007; Sutherland and McNaughton, 2000). Within this context the hippocampal cells are considered to have a “starter” and “pacemaker” role in the activation of the long-term memory formation involving columns. The fact that hippocampal cells have long-term potentiation ability and connections to thalamic association nuclei can feasibly lead to a thalamo–cortical–hippocampal–thalamo activity loop leading to consolidation. As the cortical memories become consolidated, hippocampal involvement would no longer be required. If this is the case, anatomical hippocampal connections to the thalamic nuclei (Saunders, Mishkin, and Aggleton, 2005) would suggest hippocampal involvement in all forms of memory.

The involvement of such an activity loop is suggested by the results of a study by Sperling et al. (2001). Using fMRI during the encoding of face–name associations, a consistent pattern of activation was observed in the hippocampus, pulvinar, fusiform cortex, and dorsolateral prefrontal cortex. The authors suggested the data support a distributed network of brain regions in associative learning.

Based on the current model, perhaps the best way to define memory is on the basis of the type of columnar processing occurring in each region involved. In other words, many memories employ areas distributed across the cortex and each area’s cortical columns represent specific and unique properties. There appear to be two additional dimensions related to the type of information processed and stored in the cortex.

Internal–External Stimulus Coding

During times between experimental conditions and associated active responding in fMRI studies, it was discovered that a characteristic pattern of brain activity occurred. Since the pattern was seen when no externally directed goal was involved, it was commonly referred to as the “default network” (Christoff, Gordon, Smallwood, Smith, and Schooler, 2009). The most consistent regions associated with stimulus-independent thought are medial prefrontal, posterior cingulate–precuneus, and posterior temporoparietal cortex. In a different aspect of cortical functioning, emotions have also been evaluated by neuroimaging. Medial, orbital, and inferior lateral frontal cortices appear to be consistently activated independent of type of emotion (Kober, Barrett, Joseph, Bliss–Moreau, Lindquist, and Wager, 2008). Based on such information, it is speculated that the medial cortical columns are involved with memories related internally (i.e., oneself). The default network temporoparietal involvement appears related to ongoing proximal somatosensory information which is explained in the next subsection.

If accurate, then cortical columns in regions closer in proximity to the diencephalon and limbic structures would contain memories tied to oneself, with a gradual transition to information related to external stimuli as the cortex proceeds further away from the midline. The insular temporal area in close proximity and anterior to primary auditory cortex would contain sequential sensory information related to the internal representation of oneself, with a transition toward sequential–simultaneous proceeding toward the posterior insula. Similarly, the dorsal medial parietal region would contain simultaneous, self-information, with the parietal insular area reflecting a combination of simultaneous-sequential processing.

Proximal (To Body) versus Distal Coding

The primary motor and somatosensory areas involve the most proximal-to-body columns. As the cortex proceeds away from these areas, the information becomes progressively more involved in coding distally related information. In relation to sensory information, vision and audition are the senses involved with stimuli away from one's body. In relation to the frontal cortex, there is an expected transition from columns acting upon proximal information (e.g., premotor acts upon motor columns). This would indicate the most anterior columns would be those involved with the highest order processing of non-body related information, acting upon less-organized frontal, as well as posterior cortical columns. This appears consistent with the results of a study of a reasoning paradigm adapted from Raven's progressive matrices. Golde, von Cramon, and Schubotz (2010) found that the premotor cortex became engaged in the sequential concatenation of relations, while the anterior prefrontal was involved in their integration. The authors concluded that the results support hierarchical models of frontal function.

In another study, Ranganath, Johnson, and D'Esposito (2000) found that left anterior middle prefrontal activation increased with the demands (i.e., size judgment versus old–new recognition) to recall specific perceptual information. In a study involving an analogy task, Krawczyk, McClelland, and Donovan (2011) reported the results were consistent with a hierarchical organization for relational reasoning across domains in which posterior frontal cortex is active across concrete reasoning tasks, while progressively more anterior regions are recruited to process increasingly abstract representations in reasoning.

Badre and D'Esposito (2009) indicated neurons in progressively rostral regions of the frontal cortex seem distinguished by their ability to support more abstract representations and more complex rules. This is consistent with the proximal–distal dimension and the organized-to-unorganized decoding aspect of the frontal lobe action columns as described in the dimensional systems model.

Cortical Columns as the Common Denominator in Synchronicity

Gamma-band synchronization has been an area of interest as a psychophysical hypothesis in perceptual binding since the late 1980's (Fries, 2009). The binding-by-synchronization hypothesis as discussed by Fries considers both neuronal synchronization and neuronal interactions. However, the hypothesis suggests the patterns of neural communication links allowing cortical computation are a function of segmentation and selection of input based on gamma-frequency and low-frequency rhythm. The currently proposed theory that the cortical column is the level at which cortical memory occurs provides an alternative explanation. That is, gamma-frequency input at the cortical level dynamically leads to column activation which, in its connection to other columns, is responsible for cortical computation and memory storage.

The mechanism behind this column-sized activation pattern appears to relate to active inhibition. Llinas, Ribary, Contreras, and Pedroarena (1998) used optical data from guinea-pig visual cortex using either a single electrode or two electrodes placed 2 to 6 mm apart. Stimulation with two electrodes at low frequency (10 Hz) gave rise to two waves of excitation moving horizontally and showing close to linear summation at the center of the tissue slice where they fused. Thus, the area of excitation spanned the cortical distance between electrodes. At gamma-frequency (40 Hz) stimulation, a restricted area approximately a cortical column in width was observed for each of the stimulating electrodes separated by a gap of reduced activity between the activated regions. Notably, in the presence of GABA blockade, the spatial gap activity reduction disappears. This would suggest gamma-frequency activity may well result in column activation while lower frequency stimulation results in generalized cortical activity. The end result is one which can increase the signal (column) to noise (surrounding cortex) in that gamma activity is observed in the context of low frequency (e.g., theta) recordings (Fries, 2009). The Llinas et al. findings are consistent with the previously mentioned study by Hirata and Sawaguchi (2008) in which different columns with only slight overlaps were induced by stimulation at different sites in the same cortical slice. The brief electrical stimulation leading to dynamic columnar activation would be in the gamma frequency range (50 to 60 Hz).

Another study provides support for the manner in which large neuronal assemblies can interconnect with near zero time lag synchrony. It also suggests another mechanism by which column size damage resistance can be obtained using only a limited number of neurons contained within a column. Vicente, Gollo, Mirasso, Fischer, and Pipa (2008) employed a model in which two neuronal populations relay their activities to a third population in the gamma oscillation range. The expectation was that the redistribution of the dynamics performed by this unit would lead to self-organized zero lag synchrony among the outer populations. Vicente et al. conducted simulations with networks of Hodgkins–Huxley neurons

in integrate and fire models to reflect the influence of long conduction delays. The results showed the development of the expected synchrony of the outer neurons for both a three cell circuit and a three network population circuit. The inner neurons were asynchronous. Not only does this study speak to activation speed, it also suggests that only the outermost neurons are involved once synchrony develops. This suggests that individual minicolumns and columns, when activated, synchronize only the outermost neurons while the interior neurons remain asynchronous. If correct, overlapping minicolumns which compose columns, and overlapping columns which are proposed to represent the actual information bit, can attain the required information volume to be the cortical information bit.

If the purpose of gamma frequency input is to activate a discrete cortical column, it would be expected that there should be early developmental evidence based on input from sensory thalamus. There is evidence supporting columnar activation via gamma-frequency input in the developing thalamus and somatosensory cortex. Minlebaev, Colonnese, Tsintsadze, Sirota, and Khazipov (2011) found that in postnatal days 2 to 7 with the rat, brief single whisker deflections evoke gamma band oscillatory local field potential responses in the corresponding cortical barrel. These early gamma oscillations allowed vertical synchronization between topographically aligned thalamic and cortical neurons. At the end of the second postnatal week the “adult” gamma oscillations emerge and allow horizontal synchronization in the cortex.

Moss (2006) theorized that in a feed-forward manner the location where output from lower-order columns crosses, a new column forms and then represents information from the lower-order columns. Gamma-frequency oscillations can logically be responsible for a column activating at that crossing. Repeated activation of the downstream column by the upstream columns can lead to strengthening of synaptic connections. There is some support that gamma frequency input does result in column activation across the cortex. Eckhorn et al. (1988) used fiber-microelectrodes to measure responses in areas 17 and 18 of the cat visual cortex to stimulus-evoked resonances in the gamma range. Coherent resonances were found at the minicolumn and column levels. These were also observed between two different cortical areas. In the macaque visual cortex, Berens, Keliris, Ecker, Logothetis, and Tolias (2008) also found results suggestive of columnar size activation when there was a strong correlation between local field potential in the gamma-band range and multi-unit recordings. In another study using monkeys, Liu and Newsome (2006) evaluated local field potentials and multi-unit activity in area MT in relation to motion direction and speed. Their results showed strong tuning for local field potential frequencies above 40 Hz reflects neural activity that is local on a spatial scale equivalent to or smaller than that of cortical columns.

If cortical memory involves a strengthening of synaptic connections between associated columns and, as has been suggested, the hippocampus acts to maintain

cortical activity to allow that strengthening, it would be expected that hippocampal cells would synchronize the in-line cortical columns. Obviously, gamma-band output would be necessary to maintain column-sized activity. Sirota et al. (2008) recorded local field potentials and unit activity from multiple neocortical areas (i.e., parietal, anterior cingulate, and medial prefrontal) and the CA1 pyramidal layer of the dorsal hippocampus in mice and rats. The major finding was that a fraction of neurons in different neocortical areas, in addition to spatially localized and frequency-specific gamma oscillations, were phase locked hippocampal theta oscillations. The authors believed that the data supported the conclusion that theta oscillation entrainment provides a way that activity in widespread cortical and hippocampal networks can be temporally coordinated. Another finding was that gamma oscillators were often localized to either a single cortical layer and/or a putative column. Finally, the findings were interpreted as demonstrating that hippocampal theta oscillations can effectively link the sporadic and spatially distinct local gamma oscillations.

Similar findings were obtained in the macaque in a study by Jutras, Fries, and Buffalo (2009). While recording with microelectrodes from the left hippocampus, a visual memory recognition task was performed. During the encoding phase, gamma-band synchronization was observed in hippocampal neurons and enhanced synchronization was predictive of greater subsequent recognition memory performance. It was concluded that the synchronization may facilitate synaptic changes necessary for successful memory encoding.

Using depth-EEG recordings within the hippocampus and rhinal cortex of the same nine epilepsy patients during a single-trial word memory task, Fell et al. (2001, 2003) reported on both gamma and lower frequency (e.g., theta) interactions. They investigated whether these interactions were important in encoding declarative memory. In the case of successful encoding, both structures appeared to be functionally linked by increased phase synchronization of induced gamma activity, in addition to increased phase and amplitude coupling in the lower frequency ranges. The authors suggest that rhinal-hippocampal theta coherence interacts with gamma synchronization during declarative memory formation.

In their binding of item and context model, Diana et al. (2007) provided a more precise account of the areas involved in recognition memory. Based on combined findings in fMRI studies, they proposed several aspects. First, the perirhinal cortex receives information from other cortical areas related to “what” information (i.e., specific items) needed for familiarity judgments. Second, parahippocampal cortex receives information about “where” information (i.e., context) useful for recollection judgments. Third, hippocampus receives the “where” and “what” information and binds these together to form item context associations that permit recollection. Based on the dimensional systems model, the cortical columns which project to the medial temporal lobe cortex would contain the “what” and “where” information. Although the “what” and “where” information

columns represent a high level of consolidation of lower-order columns in their respective information streams, these would be considered lower-order columns relative to the combined information contained in the medial temporal lobe columns.

Moss (2006) suggested the mechanisms, including the role of frontal cortical attention centers, by which any stimulus requiring attention is subsequently stored in long-term memory in the cortex. Based on the foregoing discussions, this can now be further elaborated to include the medial temporal lobe structures. Moreover, it has been suggested how the stimulation frequency being mediated by the hippocampus can create ongoing localized cortical tissue alterations which allow the strengthening of synaptic connections of the involved cortical columns.

It is also possible to use the gamma oscillation studies to give further insight into laterality of function. The purported global organization of columns in the right hemisphere allows less detailed and faster processing of novel stimuli. Via the interhemispheric connections, the global columns activate corresponding left hemisphere columns which can then serve as the “skeleton” outline of the developing analytical processing. The columns in the left hemisphere skeleton design can then begin the process of entraining interconnecting columns which will allow the more detailed processing characteristic of the analytical mode. Once well learned, activation of the right hemisphere columns still occurs, though the left hemisphere assumes primary control of the detailed response unless speed demands of the task negate this possibility. This would explain the observation by Borst et al. (2011) that the two hemispheres seem to have redundant functions, with most differences appearing to be quantitative (e.g., speed) as opposed to qualitative.

Integrating the Cortical Dimensions and Future Research

The relevant dimensions of cortical columnar functioning as specified by the current dimensional systems model are: unorganized–organized; simultaneous–sequential; reception–action; global–analytical; internal–external; and proximal–distal. It is now suggested that applying each of these dimensions should reveal the type of information represented in columns of specific regions. Again, there is always a distributed system going from less- to more-organized in the posterior cortex, so that columns representing lower-order information may be shared by multiple higher-order columns. The closer in proximity to the primary receiving areas, the more the columns will be shared by higher-order columns.

Information in the primary receiving areas is obviously the most unorganized. As the information stream moves outward, organization is expected to be predictable. Raw visual information in the left cortex moving dorsally along the lateral cortex would involve progressively organizing analytical, simultaneous,

external reception which will become more proximal to one's body the closer in proximity to the parietal somatosensory area. If the information stream progresses along a more medial cortical path, the columns involve internal (i.e., self-referential) information. If the information stream proceeds ventrally along a lateral cortical path, it is progressively organized and becomes more distal to one's body the closer in proximity to the temporal pole. The more medial the information stream, the more it is self-referential, but still distal. If the information moves in a horizontal direction, the columnar processing would involve both simultaneous and sequential characteristics.

Based on the foregoing descriptions, it is believed that the dimensional systems model can provide specific a priori predictions about columnar processing modes. Hopefully, this can be of benefit to researchers utilizing imaging procedures in evaluating results of their studies. Moreover, it seems possible to design studies to support or refute the model.

The probability of fMRI being used to analyze columnar processes in a more direct fashion is improving. As previously mentioned, recent refinement in fMRI methods have allowed identification of columns for ocular dominance (Yacoub, Shmuel, Logothetis, and Ugurbil, 2007), temporal frequency (Sun et al., 2007), and orientation (Yacoub, Harel, and Ugurbil, 2008), in V1, as well as motion columns in MT (Zimmerman et al., 2011). Chaimow, Yacoub, Ugurbil, and Shmuel (2011) provided further refinement in a model which can potentially be used for decoding information conveyed by cortical columns. If this is eventually accomplished, as it appears it will be, then there can be direct evaluation of the currently proposed dimensional systems model.

As was stated by Horton and Adams (2005), if it were possible to understand one part of the cortex which was representative of the whole, the task of explaining cortical functioning would be simplified immensely. We have attempted to provide a convincing argument that over 50 years ago, Mountcastle (1957) got it right. The cortical column is the basic cortical unit and it is the unifying principle for understanding cortical functioning.

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