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Review

Activation-Inhibition Coordination in Neuron, Brain, and Behavior Sequencing/Organization: Implications for Laterality and Lateralization

Gerald Young

Glendon College, York University, Toronto, ON M4N 3M6, Canada; gyoung@yorku.ca; Tel.: +1-416-726-2709

Abstract: Activation-inhibition coordination is considered a dynamic process that functions as a common mechanism in the synchronization and functioning of neurons, brain, behavior, and their sequencing/organization, including over these different scales. The concept has broad applicability, for example, in applications to maladaptivity/atypicality. Young developed the hypothesis to help explain the efficacy of right-hand reaching to grasp in 1-month-olds, a study that implicated that the left hemisphere is specialized for activation-inhibition coordination. This underlying left-hemisphere function, noted to characterize the left hemisphere right from birth, can explain equally its language and fine motor skills, for example. The right hemisphere appears specialized for less complex inhibitory skills, such as outright damping/inhibition. The hypotheses related to inhibition and hemispheric specialization that appear in the literature typically refer to right hemisphere skills in these regards. The research to present also refers to excitation/inhibition balance/ratio in synaptic function, but not to coordination in the sense described here. Furthermore, it refers to the inhibitory function widely in neuronal networks. The paper presents a comprehensive literature review, framing the research in terms of the proposed concept. Further, the paper presents a broad model of activation-inhibition coordination that can help better understand neuron, brain, and behavior, generally, and left hemisphere specialization, specifically.

Keywords: activation-inhibition coordination; inhibition; laterality; hemispheric specialization; excitation/inhibition balance; development; brain networks

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1. Introduction

Inhibition is a widespread mechanism in all living matter and life processes. As shall be shown, Go/NoGo Task behaviors, approach-withdrawal mechanisms, and excitation-inhibition cellular process balances are some of the tasks and concepts related to the question. As shall be shown, in high-order organisms, inhibition is central to these functions, including at the level of the neuron, regional brain networks, wider connectomics, and behavior. Yet, the field does not have a generic model related to inhibition that can function at all these levels and help explain them. In this regard, Young developed the concept of activation-inhibition coordination.

2. Activation-Inhibition Coordination Modeling

2.1. A Left-Hemisphere Activation-Inhibition Coordination Model

Young developed the concept to help interpret his findings (Young et al. [1]; Young & Gagnon [2]) that 1-month-olds exhibit better-coordinated arm and hand movements in reaching for a midline object (e.g., opening the hand and then contacting the object in the proper sequence and with the proper timing), even as the left hand moves about more in a nondirected fashion as if exploring the space in which the object is contextually situated. The findings of this advantage of the right hand and arm for this activity were deemed consistent with an early hemispheric specialization along adult lines, and with the left hemisphere being specialized for fine motor skills, aside from its language-related skills, and the right hemisphere for spatial and related skills.

Young attempted to find the commonalities in the language and fine motor skills of the left hemisphere relative to those of the right hemisphere, even at this early age. He was aware of standard approaches, for example, that considered it more of an analytic hemisphere compared to the synthetic right hemisphere, but considered that the refined movements in fine motor skills and language production involved a particular coordinated dynamic of precise activation with fine-tuned inhibition of interfering movements. In this regard, the activation-inhibition coordination model could accommodate the questions posed of the common nature of the function that underlies all left-hemisphere-related skills.

That is, the concept of activation-inhibition coordination enhances understanding of the central mechanism in the brain and behavior in which inhibition participates. Rather than considering inhibition in isolation, as in research on right hemisphere inhibition, or in terms of some sort of balance, as in the balance or ratio of excitation and inhibition in neuronal synaptic activity, the concept of activation-inhibition coordination is more comprehensive, subtle, and varied.

Note that the term activation-inhibition coordination is one unique to Young. Other than references to his research, the term is not found in data engine searches in psychology and related disciplines (PsychInfo, Web of Science, Scopus, Google Scholar; 28 April 2022)

As for the specifics of the concept (see Table 1), Young posited that the left hemisphere is specialized for the sophisticated, longer term, and major alterations in activation-inhibition coordinations. The right hemisphere is specialized for, or can undertake less, complex inhibitions, such as outright damping or less sophisticated activation-inhibition coordinations (e.g., brief ones, or ones requiring minor adjustments).

Table 1. Different types of activation-inhibition functions in the left and right cerebral hemisphere.

Hemisphere	Type	Description
Left	Longer term synchrony	Complex, sophisticated, interweaving (see next)
	Sophisticated synchrony	Sophisticated, subtle interweaving of activation and inhibitory skills, with appropriate activations taking place because of the suppression of interference due to inappropriate alternative behavior, both when selecting adaptive goal-directed activity and during its (movement) transitions. Both subtle competing movements and gross interfering ones are countered and controlled
	Altering synchrony	Majorly modifying/disrupting sequential activation-inhibition coordinations
Right	Adjusting synchrony	Minorly adapting/refining sequential activation-inhibition coordinations [could be left hemisphere based, depending on context]
	Long damping	Full suppression/damping activity over time
	Short synchrony	Activation-inhibition synchrony instantaneously or for a short time period. In spatial processes, some information as figure highlighted and some as ground moderated

Note: The left hemisphere specializes in a sophisticated interweaving of activation and inhibitory skills. Activation-inhibition coordination especially involves the suppression of interference due to inappropriate alternative behavior, both when selecting adaptive goal-directed activity and during its (movement) transitions (e.g., in language and in fine motor activities). Adopted from Young [3] (Table 3.1, p. 56) after adaptation from Young [4–7]. Reprinted by permission from Springer International Publishing, *Causality and neo-stages in development: Toward unifying psychology*, G. Young, Copyright 2022 (Table 3.1, p. 56).

At any level of the brain-behavior system, the neuronal firing, interregional connectivity, and complex behaviors must be: properly organized, in the correct sequence, timed perfectly, controlled for intrusion from any interfering components, target/goal-oriented, and perhaps monitored throughout, depending on the level of the species involved. That is, the activation and inhibition involved must be well-coordinated to effect these tasks in an adaptive fashion.

2.2. A Generic Activation-Inhibition Coordination Model

Figure 1 presents a diagrammatic representation of the activation-inhibition coordination process that is considered ubiquitous throughout the sequencing/organization of activity in the nervous system and its supports, e.g., neurons/ the brain and its networks, and behavior. The figure represents a sequence of activities by arrows A1, A2, and A3. The model applies to the simplest organisms, even single-celled ones, and not only advanced animals from reptiles to humans. In terms of human behaviors, the activities could be thought-related or feelings/emotions, as well as internal physiology, as well as movements/actions and social activity. The activities are prompted to action by the nature of the stimuli (S) impinging on the organism, which are referred to as configured and complex. The output (R) is similarly described. The activity takes place in context and over time, which could be micro (e.g., for neuronal firing or a task) or macro (e.g., a complex undertaking, developmental time). The activity could be much more complex than represented in the figure, such as in multitasking or in social interaction. Even the simplest single-celled organisms express applicable variations in these two examples.

The figure applies to different hierarchically organized levels or scales within the system involved. For example, in the connectome, Swanson et al. [8] found the equivalent of 50 sub-connectomes in analysis of the rat brain. The manner of their inter-organization would require the utmost coordination within the same regions and across them, including cortically and subcortically. This complex coordination would be exponentially greater in the human case. The posited activation-inhibition coordination process would appear one that is essential to the structuring involved in the connectome.

In order for proper, adaptive functional sequencing in context of activity, there must not only be appropriate activation, but also appropriate inhibition, as indicated. This refers to controlling potential and actual interferences. Activity is organized to inhibit both proximal/local and distal/global interferences. For example, the grasping hand needs to orchestrate proper sequences in the arm, hand, and fingers, while inhibiting surplus, interfering activities in these units and, at the same time, inhibiting contralateral mirror movements. Each individual activity in the sequence leads to feedback of its outcome, that feeds back into the system involved. The organism monitors the context, the goals involved, and the feedback, in order to ensure adaptivity instead of maladaptivity. Feedback could be forward or backward, that is either influencing upcoming activity or conditioning past activity to behave differently the next time. Adaptive activity reflects the quality of the activation-inhibition coordination involved. Multiple factors can upset this adaptivity—either inherent to the activation-inhibition coordination process or others external to it, such as general biopsychosocial factors in complex human activity (e.g., think schizophrenia, child abuse, poor motivation for whatever reason). The figure depicts an inhibitory plasticity, which involves more than suppressive inhibition because the plasticity involves a reciprocal balance in activation/excitation (inhibition) in order to maintain homeostatic stability, which is the role of inhibition in classic models.

Figure 1 graphically presents a simple sequence of activity in terms of activation (+) and inhibition (−) signs. The figure can be translated into network concepts [9] by considering the arrows as nodes and the + and − signs as links (edges). Given the complexity of behavior and its individualization, the activation-inhibition coordination networks for any one activity for any one individual will be exceedingly complex, with different nodes, links, strengths, centralities, drivers, etc.

According to Young, different types of maladaptivity can result from different lacks in the exquisite synchrony required in activation-inhibition coordination as presently defined. For example, he noted that, in Attention Deficit Hyperactivity Diosrder (ADHD), inhibition difficulties are considered critical underlying factors, and perhaps those difficulties can be reworked in terms of the concept of activation-inhibition coordination. Similarly, the disorder of schizophrenia has been described in terms of deficits in inhibitory capacities, even in terms of underlying impairments in inhibition-related interneurons and the inhibitory neurotransmitter GABA.

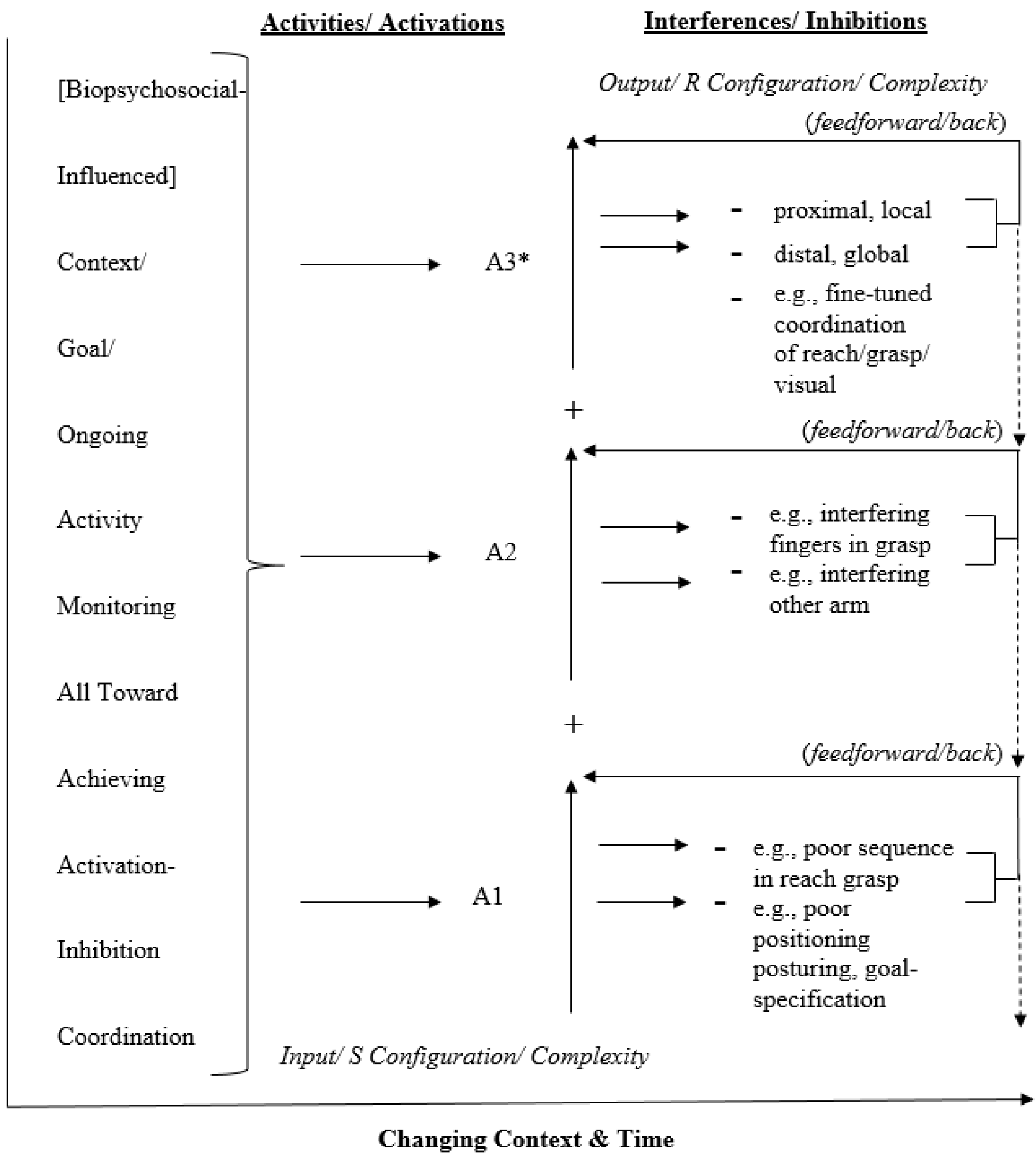

Figure 1. Mapping activation-inhibition coordination. The figure specifies an activation-inhibition coordination model that helps explain functionality at multiple scales, from neuron to brain to behavior, and their sequencing/organization. The coordination can be developmentally disturbed, go awry for multiple reasons at multiple junctures, producing aberrant activity. The modeling depicts an inhibitory plasticity, and more than inhibition as a reciprocal balance to activation/excitation in order to maintain homeostatic stability, per classic models. The model can apply to other levels in living function, for example: (a) in the genetic transcription process in which ordered activity is essential; in DNA activity; (b) when epigenetics inhibits promotor regions of DNA; (c) in single-celled animal function, in which behavior needs to be sequentually coordinated for adaptation. * Refers to sequence/organization in: (a) cellular/neuronal firing, (b) neurological/subcortical-cortical activity, and/or (c) behavior (thoughts, feelings, movements, physiology, relational/socialization).

Whether looking at neurons or other neural/neurological activities, smooth coordination of activation and inhibition components is essential for adaptive functioning, and their disorganization in these regards can lead to maladaptivity/dysfunctionality/disorder. Young did not specify exactly how the activation-inhibition coordination might differ from one disorder/dysfunction to the next, and this remains a long term goal for work with the concept. Moreover, there are multiple scales involved, and cascades from one scale (e.g., cellular) to the next (ultimately to brain and behavior), complicate the project. That said, the literature review below does give some pertinent examples.

Generally, maladaptive behavior could be described in terms of: (a) excessive inhibition/suppression; (b) excessive unchecked activation; or (c) problems in the coordination of activation and inhibition. The various externalizing disorders, for example, appear to reflect an absence of the required inhibitory control, as does manic-related ones, while unipolar motivational, depressive internalizing disorders would appear to reflect an excess of the inhibition function. Coordination difficulties in these regards could manifest multiply in individual ways, for example, depending on individualized biopsychosocial impacts and vulnerabilities.

3. Clarifications

In the following, I address the major concerns of the reviewers. In essence, they asked for: (a) better conceptual clarity; (b) more on prediction/testing/falsifiability; and (c) better differentiation of the model over different scales developmentally, brain-wise (e.g., neuronally, connectomes, hemispherically), and in its application to individual differences/maladaptivity. They asked whether the model is too broad and imprecise to apply to interpreting or reworking other models, concepts, and research (e.g., approach vs. withdrawal).

3.1. Definitions

Coordination. I checked multiple online dictionaries, added my own comments, and arrived the following. The definition is expansive in order to include all dynamics and scope involved for present purposes.

Coordination is a complex characteristic of complex systems having two or more elements or units. The system could be a structure or activity. It could be internal, as in thought (at least for more complex systems, humans included), or external, as in action (which would apply to all possible systems). It could be about one system or over several or more. It could be superordinate organismic systems, or across organisms. It could be supra-organismic, as in social and political organizations. At a more complex level, it refers to a process of organizing or orchestrating the different elements/units of the system. At a simpler level, it refers to arranging or putting together the elements/units. There could be simultaneous processes involved, or sequential ones, or both. If accomplished well, the elements/units become superordinately balanced or harmonious in their relations. The coordination allows for collaborative control efficiency and effectiveness when done well. More simply, the units/elements work together smoothly, and the system internal organization, or its output, or both, are more functional/adaptive than would otherwise be the case.

In terms of how the definition of coordination applies to the concept of activation-inhibition coordination, even when considered separately, inhibition and activation are powerful processes in the structure and activity of systems. However, without their proper coordination, the system risks not being organized, efficient, and adaptive, with waste of energy/effort, and less effective action, thought, etc. Activation-inhibition coordination conditions entropy in the system, allowing for more graceful, smoother, less energetic adjustment to ongoing context, demands, needs, and efficacy requirements. In these senses, coordination is not just balance, because it implies a superordinate level to the system in which the components/units create a new level in the system involving greater sophistication pursuant to improved contextual adaptation. This is the reason why activation-inhibition coordination is a generic process that is present throughout all tiers of an applicable system, and, indeed, in any functional system, to the extent the context and the system properties allows it.

There are limits and difficulties in the process of effective activation-inhibition coordination. The system involved will have inherent limits on the number of units that it can effectively coordinate. The more complex the organism, the better the possibility of complex activation-inhibition coordination processes. The quality of the coordination could vary from one system to the next, or one organism to the next. A host of factors can affect that quality, from the collective biopsychosocial in the human case to more generic structural, relational, and ecological factors. That is, to generalize the biopsychosocial model to all organisms or entities, from the human, including in their complex social and political organizations, to the simplest, e.g., one-celled life forms, the systemic factors that can affect system output could be referred to as structural-relational-ecological.

Inhibition. Inhibition is ubiquitous in behavior, but its definition has been questioned and its bracket creep as a concept noted. Werner et al. [10] noted that, at the broadest level, inhibition has been defined as "any mechanism that reduces or dampens neuronal, mental, or behavioral activity" (Clark [11], p. 128). They gave further definitions that have emerged in the field that are too vague, imprecise, or dilute and overextend the concept. At the human behavioral level, they gave the definition of inhibition in terms of outcome rather than process, for example, in terms of strategies used to control unwanted impulses and desires.

As much as the approach to reconsidering inhibition as an outcome rather than a process (and an outcome that is actualized by the strategies people use to achieve inhibition) addresses important issues, my concern is that the proverbial baby has been thrown out with the bathwater. First, the broad definition of inhibition needs to apply to more than the human case. Second, the authors did not criticize the broad process definition they offered, taken from Clark. Third, by revising that process definition to be more inclusive of their concerns, the process approach can be improved and the definition of inhibition in this sense made more viable.

In this sense, inhibition can be defined as any mechanism that stops/dampens, contains/controls/modulates the activity of its process, and/or reduces interferences on or disruptions of ongoing neuronal, brain-related, or behavioral activity. In the human case, often this is understood as goal-directed or target-oriented, and also in the case of other organizational structures, e.g., in higher-order human institutions. This broad definition includes cognitive strategies in the human case that might be used to arrive at the inhibition, allowing for the desired/wanted/targeted outcome of inhibitory-related regulation of the activity. This definition is consistent with the present approach of activation-inhibition coordination taking place as a causal mechanism of behavior and related supports (e.g., neuronal, brain-related in the human case) at the broadest levels.

3.2. Prediction/Testing/Falsifiability

Hemispheric Specialization. Table 1 specifies how the model applies differentially to the hemispheres, and it leads to specific predictions in this regard. Furthermore, it can be extended to apply to how adaptive vs. maladaptive behavior might look. In short, many of the concerns in this section are accounted for by Table 1.

According to the table, as applied to hemispheric specialization, activation-inhibition coordination can take multiple forms, but the most advanced forms relate to maintaining a continuous, organized sequence in behavior at the micro-level, with ongoing moment-to-moment organization to meet adaptive goals. The left hemisphere is considered the seat of this specialized complex ongoing behavior. The left hemisphere manifests this skill in terms of its primary behavioral specializations, which include speech, manual manipulation, and related activities.

A good way of testing the model would involve kinematic analysis of verbal behavior, communicative gesture, and bimanual coordinations, either separately or together. The kinematic analysis would specify the applicable linkages in the sequence of behaviors involved from one movement to the next at the microsecond level, while indicating the way in which interfering movements are contained/controlled, or not, in an overflow/mirror fashion.

Furthermore, the model posits that complex social interactions require these skills, in that the sophisticated synchrony in activation and inhibition coordination inherent to the behavior would call for, in the proper context, the posited advanced left hemisphere activation-inhibition coordination skills. This type of hypothesis is consistent with the left hemisphere approach (vs. withdrawal) model. Approaching is more sophisticated than withdrawing, generally, given that, often, withdrawal would include social isolation, retreating using short term activation-inhibition coordination, at best, etc.

What if the social interaction is so complex in the sense that it involves ongoing dynamic behavioral and verbal interactions? Here, the context could dictate the left hemisphere engages the most sophisticated portion of the social interaction, such as the verbal one, and other components of the interaction are shunted to right hemisphere control rather than overcrowding the left hemisphere, depending on the network reserve available in the hemisphere for the interaction at hand. Or, the left hemisphere can coordinate as dominant in the activation-inhibition function with the right hemisphere, which will have a subservient, complementary, less complex role in the function. Finally, one particular behavior might invoke left hemisphere activation-inhibition coordination skills in one context, but right hemisphere ones in this regard in another. It would depend if the associated (second) behavior for the task is easier or harder than the index one. These types of conjectures are ripe for experimentation and refining the model in question.

In another example, face perception has been shown to be a right hemisphere specialization, but perhaps because other social skills in interactions require advances left hemisphere activation-inhibition coordination skills and face perception is lower-order in this regard (so is shunted to the right hemisphere in this context). Similarly, the mother might cradle the baby on the left side to engage the right hemisphere for the facial dynamic exchanges involved in the interaction, but, as well, to free the right hand (left hemisphere) for the ministrations required in caring for the baby on an ongoing basis while it is held (e.g., see Herdien et al. [12], for this possibility). The relative advantage posited for the left hemisphere for more complex social and ongoing interactions is supported by the finding that the type of emotions processed with a right hemisphere advantage are more negative than positive (e.g., see Hartikainen [13]). These types of predictions are large-scale, and kinematic analyses might show the fine-grained points in the interactions when the sophisticated activation-inhibition coordination skills posited for the left hemisphere apply well.

Maladaptivity/Atypicality. Different inhibitory deficits have been associated with different mental/behavioral disorders/conditions. As demonstrated above, developmentally, ADHD is prominent in this regard. For psychopathology, schizophrenia has been associated with inhibitory deficits over multiple scales. The manner in which these findings can be extended to difficulties in activation-inhibition coordination is difficult to specify exactly, without the basic research not having been undertaken in this regard. The basic research could take place in terms of: behavioral kinematics seeking activation-inhibition coordination dynamics and their problematic expressions; actively seeking patterns in symptom networks that reflect this function; and seeking similar patterns in brain network dynamics, including in terms of the major ones of executive function, salience, and the default model network (DMN; Ma & Zhang [14]).

Connectome. The brain is massively organized and networked into structural and functional units, often referred to as units in the connectome, intracortical networks, tract interconnectivities, etc. Neurons form internetworks from the earliest phases in development, even in the simplest organisms. The adaptive functionality of the brain or neuronal networks, as the case may be, depending on the complexity of the organism, as represented by the successful goal-directed behavior of the organism, speaks to the complex organization involved, and asks for proper explanatory mechanisms in the functioning. It is circular to say the connectome or intracortical network accomplishes or is "responsible" for the task involved, as deeper explanatory mechanisms are required. These mechanisms could be more distal, as in genetic underpinnings, or more proximal, as in the proposed activation-inhibition coordination.

Scale. How could one mechanism apply to the extreme differences in scale involved, from the lower-order individual neuronal activity, to their linkages and circuits, to upper-level intra-cortical networks, connectomes, etc., keeping in mind that even the latter will have hundreds if not thousands of sub-connectomes. The inverse question would ask how could diverse, dispersed, less economical proximal causal mechanisms be involved over different scales of a system instead of a superordinate one that cuts across the different scales of the system in the individual organism, including over cross-organism organization. Nature abhors a vacuum; as does science, and mechanism in both these cases, the concept of activation-inhibition coordination offers a compelling, even if as yet not empirically tested mechanism, for the organization involved.

What are the alternatives to cross-scale explanatory mechanisms in neuron, brain, behavior, and their organization? Do approach-withdrawal processes work? Not really, because they too require explanation beyond the simple case of one or the other component being in play. Does anything related to goal processes work, such as being on target or not, and the like? Not really, because how are target and non-target behaviors and processes themselves integrated for successful adaptive functionality?

Moreover, having one common mechanism that cuts across different scales of the system does not imply that they coordinate the components involved in the same way. Neuronal coordination is not the same in terms of brain network coordination or behavioral coordination, for example, in terms of contents. However, the underlying process remains the same despite content differences over scale. The same applies to the different contents in different organisms, different systems, e.g., the individual, the extra-personal institutional unit, and any other variation in this regard. The latter proviso includes developmentally.

Development. The cohesion afforded by one constant organizational principle that establishes neuronal, brain, and behavioral coherence, efficiency, and efficacy allows for a more adaptive growth process that can accommodate fast-changing transitions in behavior and neuron/brain. The latter conjecture is another area that would provide fertile testing ground for the hypothesis. To argue that activation-inhibition coordination cannot apply equally to different states of complexity in the growing organism misses the point that the proposed mechanism is a generic. universal one over scales yet allows for individual differences and maladaptivity/atypicality at the same time.

Networks. Borsboom [9] has developed the concept of networks as applied to symptoms, for example. It involves calculating correlation-based statistics on the linkages (edges) among the units, which are referred to as nodes. Symptom clusters do not represent latent structures; for example, the symptoms of PTSD are causally linked and act causally, and there is not a superordinate diagnostic entity that represents them. Critical nodes are considered drivers of others causally, as in poor sleep. Node clusters can be more central, coherent, cohesive, or more widely distributed and less tight, a concept that can be used to characterize left vs. right hemisphere function, for example.

Young [15] modified network theory by creating a hybrid model that included systems theory, which allows not only for symptom configurations but also for superordinate levels that can act down on symptoms. The top-down levels acting on the bottom-up ones would be akin to diagnostic categories, for example, PTSD, but individualized for the person rather than representing a uniform diagnostic category in a manual. The levels involved would mutually influence each other. Moreover, causality in the full system involved, then, would reside in more than symptom interactions and their links and causality drivers, and also even include individual appraisals, such as about the severity of the instigator trauma and the resources available to cope with it.

In terms of the applicability of the concept of networks as elaborated by Young [15] to the concept of activation-inhibition coordination—collectively, the network concepts of nodes, their linkages, specific causal drivers, superordinate levels of the system that emerge from the unit interactions and act downward to influence them, and vice versa—networks are conceived as organized in terms of activation, inhibition, and their coordinations [3]. Correlations are statistics that need explanations of their underlying connectivities and psychological relationships. Traditionally, networks are considered in terms of activations and not inhibitions, but networks needed to be considered from the multiplicity of types of activations, inhibitions, their coordinations, and disturbances/nonnormalities in this regard. The concept of networks in the Borboomian sense, and especially as modified here, is exquisitely applicable to individual differences and psychopathology, for example. As well, the combined hybrid network-system and activation-inhibition coordination concept, as proposed here, applies equally well to the different scales being discussed, including developmentally. Just as network theory has a burgeoning body of empirical research in its support, its extension into systems/different levels/different scales. Applying the activation-inhibition coordination concept to it, as proposed here, is workable, allows for predictions, is testable, and is falsifiable, as any proper modeling would require.

Implicit in the present approach is that causality exists at multiple levels, and not just the distal-proximal dimension. Just as genetics distally includes the various -omics, and epigenesis (e.g., DNA methylation due to early stressful experiences), proximally, the activation-inhibition concept needs to be complemented in understanding behavioral expression by different explanatory models, such as the biopsychosocial one (or structural-relational-ecological one), as described.

Breadth. A reviewer noted that, post hoc, the activation-inhibition model appears to explain anything and everything, so it not testable or falsifiable. To this point, I have indicated how the model can be applied, and the specific types of predictions that can be made using it, as well as the methodologies to operationalize them. Moreover, as just emphasized, the activation-inhibition coordination concept is nested in multiple causality concepts at different hierarchical levels, and so, by definition, cannot explain everything and anything.

The reviewers also noted that, problematically, potentially falsifiable evidence can be re-interpreted to support the proposed model, rendering it untestable; it is too flexible. In this regard, I note that key sets of concepts/models and data/evidence that support any theory relate to those derived from competing and prior theories in the sense to the degree they can be reworked to fit the new theory in the theory building process, while surpassing in explanatory power the other models that attempt to explain similar phenomena. Furthermore, the new model should help explain inconsistencies in other models, fill in their missing gaps, make testable predictions not possible in the other models, extend them into uncharted territories, e.g., over different domains and scales, and overall, give more coherence and elegance in the applicability of the model to its field. In this sense, reworking other models in terms of those that attempt to build on them is part of the accepted model building process and the validation of any new model. The key controls in this regard relate to explaining better extant data and data deriving from new predictions afforded by the model, and explaining better inconsistencies in the field, whether conceptual, empirical, or both. As theories build toward more inclusivity this way, the risks of trying to explain everything and anything are palpable. However, the inherent controls in the theory construction process offer criteria that either strengthen them or, at the other extreme, render them too imprecise to be contributory. The present activation-inhibition coordination concept of causal explanation of neuron, brain, behavior and their organization has been constructed to be open to being tested by the mentioned controls to model building.

In the end, activation-inhibition coordination refers to the units in the system being regulated by the processes of activation, inhibition, and their coordination, but what if the units themselves undergo changes in system development? For example, neurotransmitters change their postsynaptic consequences during development, e.g., GABAergic interneurons start out excitatory, then shift to inhibitory. For the general process involved of activation-inhibition coordination, these types of changes do not complicate understanding or application of the model; it is a generalized one that overarches specific components of the system involved, whether neuronal, brain-wide, developmental, or behavioral, as should be evident by this point. Similarly, the generic process of activation-inhibition coordination as applied to different scales will not be complicated by different activatory and inhibitory processes at the different scales, different types of activations and inhibitions anywhere in the system involved, and so on. Furthermore, in this regard, the mechanism is not inconsistent when inhibitions serve to activate behavior, activations serve to inhibit them, and so on. Neuronal inhibition could activate higher-order networks, and vice versa, and the activity of a network could contribute to activation or inhibition of behavioral expression.

3.3. Interim Conclusion

To this juncture, at the general level, the paper has presented the primary elements of the present activation-inhibition coordination model as an explanatory mechanism across scale, including developmentally and evolutionarily, in the orchestration of complex neuronal, brain-based, an behavioral sequences. Furthermore, the paper has elucidated how the model applies to differentiating the foundational specializations of the left and right brain hemispheres, with the left hemisphere considered the seat of the most complex, sophisticated organizations in this regard. At the same time, the model acknowledges that complexity along these lines varies with context/task, age/development, the species, and so on. Moreover, the contents of the activations, inhibitions, and their coordinations will vary over the different scales, e.g., developmentally, over species, over levels (neuron, brain, behavior), and the organizations involved in context/task. This does not present a problem for the model, making it too broad. Too the contrary, it emphasizes its scope, while specifying its predictability/testability/falsifiability.

The following literature review provides some critical supportive research on the activation-inhibition coordination concept as found in Young. Young (e.g., [3]) had examined supportive research but he found little that speaks directly to the question, given the novelty of the concept for understanding the sequencing/organization in neuron, brain, and behavior. That is, the research that Young had cited to date related to the concept addresses it indirectly, although is consistent with it. Once the relevant literature in Young [3] is reviewed below, the more recent literature is reviewed on the question. Here, research that is more directly on the concept of activation-inhibition coordination is emerging.

4. Literature Review

4.1. Past Relevant Literature in Young (2022)

Ratnarajah et al. [16] studied structural connectivity of the neonate brain, and noted asymmetries that are consistent with the activation-inhibition coordination hypothesis of left hemisphere specialization. They used diffuse tensor imaging (DTI) scan methodology, and focused on white matter axonal pathways. They found more efficient left hemisphere structural connectivity, as indicated by better left hemisphere intra-regional integration and better "between centrality" connectivity. The authors concluded that the left hemisphere appears to function with more efficient circuitry, which allows quicker information transfer and flow. These functional differences in the hemispheres at birth speak to the hypothesis that the brain is specialized for its functions right from birth and that the specialization involves a generic activation-inhibition coordination skill.

Shine [17] described integration and segregation of cortical networks in the brain, and these appear similar to activation-inhibition coordination. Functionally segregated brain networks consist of networks referred to as "small worlds," in which tightly intra-connected modules link weakly to other networks. In contrast, functionally integrated networks form modules that are not as clearly intra-organized, but they are more interconnected with other ones.

According to Shine [17], neuro-modulatory systems modulate the "equilibrium between excitation and inhibition in the network" (p. 574). The cholinergic system functions to increase network segregation. The noradrenergic system facilitates cortical networking integration. The two systems also are active in balancing the sympathetic and parasympathetic systems; and network dynamics underwrite other function through their segregation and integration, e.g., in learning complex motor sequences. Much like the concept of activation-inhibition coordination, the similar one of integration and segregation of cortical networks and associated neuromodulatory systems appears to have widespread currency in brain and behavior. The activation-inhibition coordination model adds value to the integration-segregation one by providing a mechanism for the equilibrium it purports to maintain.

The literature review that follows on recent publications that speak to the activation-inhibition coordination hypothesis on neuronal, nervous system, and behavior and their organization informs the concept greatly. The review cannot be exhaustive, because there is so much work on excitation-inhibition related to neurons, left hemisphere inhibition-related skills and right hemisphere damping inhibitory skills, as well as multiple behaviors that could be recast as expressions of activation-inhibition coordination. The take-away from the review includes that there is better understanding of inhibition and its role in activation and plasticity in multiple integrative concepts at all these levels, including in cortical and behavioral networking.

4.2. Recent Relevant Literature

4.2.1. Neuronal

Gandolfi et al. [18] referred to inhibitory interneurons as providing global neuronal circuit stability, controlling their synchronization, and contributing to neuronal firing. They described inhibitory synaptic plasticity as being critical in proper functioning along these lines, and contrasted this recent view with the classic one. In the latter view, excitatory connections constitute primary adaptive drivers in learning and memory related circuits, while inhibitory ones were considered as their "fixed controllers", with "substantial invariance".

In the more recent view (per Gandolfi et al. [18]), inhibitory-related synapses are considered "responsible" in the formation of complex states of the brain, based on the activity of their molecular and cellular mechanisms. Inhibitory synapses become altered in both long term potentiation (LTP) and depression (activation and inhibition, respectively, to use present terminology). The excitation/inhibition balance in synaptic activity conditions inhibition plasticity, and has effects in altering neuronal circuitry and consequent learning and memory. Long-term GABAergic dysregulation, in this regard, is associated with neuropsychiatric disorder.

However, these authors maintained that a precise definition of balance along these lines is lacking. What is the mechanisms in the interplay between excitatory and inhibitory signaling? For example, research now reveals that the balance in GABAergic and glutamatergic synapses is crucial in the timing of neuronal cell spike generation (e.g., Wehr & Zador [19]). The task of elucidating the dynamics of inter-neuronal inhibitory activity is complicated by their multiple classes and subclasses of different types (e.g., chandelier vs. basket cells have different innervations along the contact principal neuron). GABAergic interneuron classes include: ParValbumin, cholecystokinin, SOMatostatin, and serotonin receptor 5-HT3A, each with different effects, e.g., in presynaptic, postsynaptic, or mixed effects. The authors moved on to discuss the functional role of inhibitory synaptic plasticity, and referred to homeostatically regulating excitatory/inhibitory balance. This might take place by reducing feed-forward excitation/inhibition or by increasing inhibitory neuron activity. For example, Haas et al. [20] found that, for the entorhinal cortex, inhibitory connection strengthening helps block excitatory wave propagation, which preserves network stability.

Tatti et al. [21] actually referred to coordinated or coregulated signaling pathways for GABAergic and glutamatergic transmission, which is consistent with the present activation-inhibition trans-scale coordination model. They further elucidated the nature of the coordination involved and how excitation/inhibition (E/I) balance dysregulation impacts conditions, like Rett's syndrome, schizophrenia, autism, and epilepsy. They noted that the majority neocortical E neurons synapse both locally and globally, with the latter allowing projections to distal targets cortically, subcortically, and to the brainstem. In contrast, GABAergic I neurons connect only locally, and are primarily pyramidal.

According to Tatti et al. [21], both E and I neurons organize modularly to help signal processing. Specifically, neurons in the neocortex create arrays referred to as descending mini-columns, with the E and I neurons forming the core of the mini-columns. I neurons within a mini-column connect both within and between layers. Other I neurons are flankers, and allow lateral inhibition, thereby modulating any signal propagation across mini-columns. Within mini-columns, different I neurons balance the E neurons: ParValbumin-positive ones are wide-arbor basket/chandelier cells that function to inhibit the activity of neighboring mini-columns. In contrast, calbindin/calretin positive double bouquet cells function inhibition-wise via translaminar synapses. These various cellular inhibitory functions within and between mini-columns provide the basis for E/I synaptic and neocortical balance. This balance refers to the neurons working together in signal processing and feature detection (network gain, response tuning, cortical activity stabilization by inhibitory control). In other words, the coordination suggested is indicated best by achieving the goals of the system involved, which is consistent with present formulation. As for similar research, in motor coordination, tonic inhibition facilitates the coordination involved, a process which includes astrocytes in the cerebellum that release GABA for this function [22].

Another area of brain function that involves activation-inhibition at the molecular level concerns concussive head injury (CHI). Sharma et al. [23] referred to dysregulation from CHI in the central nervous system's (CNS) endogenous balance of E and I neurotransmitters, which is at the root of CHI's brain pathology. These effects include neuronal, glial, endothelial, and axonal degeneration, which contributes to CHI symptomatology. E neurotransmitters include aspartate and glutamate. The I neurotransmitters glycine and GABA work to counteract the excitatory ones, and this compensation is accentuated in CHI in order to neuro-protect against cell injury after CHI. For example, excess release of glutamate following CHI leads to excitotoxicity (e.g., via intracellular accumulation of Ca^{++}) and subsequent neuronal injuries, cell death, etc. From a developmental perspective, Schmidt et al. [24] found an association between pediatric concussion and delayed onset of interhemispheric inhibition.

Herstel and Wierenga [25] elucidated a concept of brain network control through "coordinated inhibition". They argued that proper brain function requires coordinated excitatory and inhibitory activity. This conceptualization of adaptive dynamic brain activity speaks directly to the present concept of activation-inhibition coordination in these regards. The authors provided a two-photon limit microphotograph of a dendrite of an excitatory CA1 pyramidal cell and an inhibitory axon interacting, to illustrate the concept. They referred to excitatory and inhibitory plasticity co-occurring within dendrites in this regard. The authors indicated that, in the image, once local glutamate uncaging took place at excitatory synapses, they developed plasticity at several spines, as well as a new inhibitory presynaptic bouton at the locus where the axon crosses the dendrite. The authors concluded that this indicates "local crosstalk" over excitatory and inhibitory synapses.

As with others, Herstel and Wierenga [25] contrasted the classic approach in which cellular networks inhibition was considered part of a reciprocal process that acted to maintain system equilibrium or homeostasis. They referred to E/I balance in this regard, and even that it involved coordination of activation and inhibition ("proper functioning of neural networks in the brain requires coordinated actions of excitatory and inhibitory synapses" (p. 34)), but added that the concept of balance is ill-defined, which is similarly maintained in the present approach.

According to Herstel and Wierenga [25], the more recent view is that inhibition is a plastic driver or rule controller in the equation of E/I balance, such as in neural network changes in memory. Sensory information processing in the brain is controlled by inhibition linkages. It takes place in conjunction with inhibition-stabilized networks having recurrent excitatory and strong inhibitory counteractive connections that inherently act to counter perturbation after stimulus-induced instabilities in the system. The E/I balances here are variable, for example, relating to network activity and context, in which gain control mechanisms might be involved. Research reviewed suggested to the authors that learning involved network reconfigurations by dedicated change in inhibitory circuitry. The paper concluded by indicating that GABAergic-driven inhibition has the "power" to affect when and where excitatory activity can take place, despite the fact that inhibitory synapses are quite in the minority.

He and Cline [26] also referred to E/I balance in neuronal activity. They described that coordinated excitatory and inhibitory inputs in neurons and circuits act to establish and maintain the proper E/I ratio for their adaptive function and stability. However, they considered the E/I ratio as imprecisely defined. They pointed out the many variations involved, and that the excitatory component is more the driver, with the inhibitory component reactively re-establishing the required ratio. In this regard, they differed from Herstel and Wierenga [25], and further research is warranted. Either way, in the present view, the coordination of E/I in multiple ways is responsible for cellular and neuronal circuitry stability and function, with the E/I balance being one of them.

Kajiwara et al. [27] examined the cortical micro-connectome in terms of activation-inhibition balance. They noted that there are more excitatory neurons than inhibitory ones, yet they keep balance. They found that inhibitory interneurons have more controlling abilities than excitatory ones, accounting for the compensation. This argument is similar to the one of Herstel and Wierenga [25].

To conclude, the present activation-inhibition coordination concept does not refer only to a correct balance or ratio in activation/excitation and inhibition/suppression, because the balance/ratio index does not speak to the coordination required for adaptive function. Coordination is a global function that does not mean only homeostatic balance in E and I functions, but more, as per Figure 1.

4.2.2. Cortical

Indeed, workers are referring to the "inhibitory connectome" in brain networks (Rumpel & Triesch [28]). For the latter, because of inhibition, the connectome is dynamic, and learning induces temporary synaptic "disbalances" that do not progress into pathological excitability.

For Fortel et al. [29], excitation-inhibition dynamics can help unify understanding of brain structure and function. The authors presented a maximum entropy model that applies over the various scales of the systems involved, and address nonlinear dynamical criticality models. The model is too complex to present here, but it illustrates the collectivity function in neurons and the thresholds that trigger their action. Perhaps an index of the activation-inhibition coordination dynamic might represent the critical threshold function precipitating system change (the critical variable or control parameter at which the system changes). When the critical threshold of the control parameter is attained, that triggers regime changes, or, if it is not reached beyond threshold, the system preserves its stability, everything else being equal.

Adesnik [30] argued that the different layers of the primary visual cortex in the mouse's brain are maintained in balance by neuronal synapse activity balance in E/I. These balances act to stabilize activity within layers, but contribute dynamically to drivers downstream in other layers, including through gamma band activity. The result is that the E/I balance and the propagation that results over layers "shape" information flow through cortical circuitry.

In an article on connectome harmonics, Atasoy et al. [31] presented a neural mechanism underlying the self-organization involved in terms of a continuous neural field model of E/I interactions. As already discussed, excitation in these regards is mediated by glutamatergic principle cells and inhibition via GABAergic interneurons. The neural fields created are related reactor-diffusion models of mutual interactions between a diffusing activator and inhibitor, which lead to self-organizing pattern formation. The excitation is short range and the inhibition broader and lateral, leading to center-on/surround-off connectivity, as found in the early visual cortex.

All these articles address the concept of activation-inhibition coordination in neuron and brain, and consequently for behavior. Some do so more directly, but the present concept integrates them beyond their contributions.

4.2.3. Disturbances in Behavior

Migraines have been related to E/I imbalances in the cortex. In a visual cortex study, Nguyen et al. [32] supported that, in migraines, cortical hyperexcitability (in present terms, hyper-activation) drives an E/I imbalance, leading to increased local inhibition.

Rett's syndrome, which is a profound neurodevelopmental disorder, has been characterized in terms of E/I imbalance across multiple scales [33]. E/I imbalance in Rett's is a fundamental mechanism in dysfunction in cellular and synaptic processes, and it varies with brain region and cell type. For example, postnatally, dynamic synaptic E/I balance facilitates adaptive spatial and temporal neural circuitry modification, and the dysregulation in Rett's involves this early E/I balance. Furthermore, in Rett's, there is hyperactivity in the motor cortex related to GABAergic activity dysfunction [34]. There is dysfunctional E/I imbalance in the hippocampus, with GABA and interneurons implicated. Similar perturbations are involved in the brainstem, among other areas.

For autism, research reveals dysfunctionality in global network organization in the macroscale connectome manifold, in terms of E/I imbalances [35]. Specifically, in this neuroimaging study, the authors found associations with increased recurrent E/I and excitatory sub-cortical drive in the autism sample relative to controls. Furthermore, see Rohr et al. [36], in another neuroimaging study, for a shifting inhibition function in autism.

ADHD is another condition in which maladaptive inhibitory processes have been implicated as a causal mechanism. According to a study by Luo et al. [37], in sequential left or right unimanual finger tapping tasks, during the nondominant hand finger tapping trials, children with ADHD relative to controls exhibited more involuntary, mirror overflow (non-tapping hand) movements. From the ADHD children's simultaneous EEG results, the authors referred to altered cortical activation/worse inhibition in the ipsilateral hemisphere through corticospinal tract (ICT) non-decussating fibers originating in the sensorimotor areas. Here, we have a more exact mechanism proposed in relation to the voluntary motor movement inhibitory difficulties of ADHD children, which implicates a deficient inhibitory mechanism, more often than not in the right hemisphere.

At the other end of the age spectrum for finger tapping, hemispheric differences disappear in the older population [38]. Similarly, for a stop-signal task, Paitel and Nielson [39] found that, in the younger sample, there was more right- than left-hemisphere inhibition, unlike in the older sample, which behaved bilaterally in the P300 measurements undertaken. These studies demonstrate that there might be age differences in activation-inhibition coordination in the elderly compared to younger individuals, for example, related to recruitment of the left-hemisphere for the function as part of age-related compensation strategies.

4.2.4. Lateralization

Research is specifying better the left hemisphere fine motor advantage, and relating the left hemisphere to better inter-coordination hemisphere skills. The following presents research supportive of the left hemisphere advantage for complex inhibitory skills.

Motor Skills. Ishibashi et al. [40] found that, in rapid movements, the left hemisphere engages better in contralateral inter-hemispheric inhibition and appears specialized for rapid and sequential movements, in this case of the simple variety. Specifically, the authors used interhemispheric signal propagation (ISP) toward evaluating interhemispheric connectivity in movements that tapped the primary motor cortex (rapid abduction index finger tapping in response to a stimulus). The study results specified that the left primary motor cortex more strongly inhibited the homologous area in the right hemisphere during right-hand rapid movement compared to inhibition from the right primary motor cortex to the left one during left-hand rapid movement. It was noted that these results complement the findings of similar studies using sequential movements.

Developmentally, Bondi et al. [41] gave dexterity and speed tasks to 6- to 11-year-olds, finding that right handed children excelled with the right hand on the dexterity task. They inferred that the left hemisphere is specialized for "complex coordinative" behavior. The dexterity task was a role-differentiated bimanual one, with one hand inserting floppy disks in their proper cases one at a time (and as quickly as possible), with the other hand "controlling" the cases. The speed task involved the thumb touching the other fingers of the same hand (fingers 2, 3, 4, 5; and then in reverse). The authors did not refer to the model of hemispheric specialization supported by the findings, but right hand coordinative dexterity supports an activation-inhibition coordination model in the left hemisphere, as presently argued.

Reworking Other Models. Connectome research is confirming the differential organization of the left and right hemispheres in terms of network connectivity. In this regard, Avena-Koenigsberger et al. [42] referred to better integration and segregation in the left hemisphere compared to the right, as determined by k-shortest path ensemble data from diffusion imaging and tractography. Integration-segregation differences in anatomical structure could provide the underlying structural basis for the functional differences hemispherically, which speaks to the concept of activation-inhibition coordination, as potentially underwriting the integration-segregation findings.

The integration-segregation model was applied to understand the functional connectome of neurodevelopmentally at risk children by Jones et al. [43]. They found altered patterns in these children relative to controls in this regard, with some expected integration not present and some expected segregation not present. This research is consistent with Shine [17], described above, and my interpretation of the integration-segregation model as one which the activation-inhibition coordination model can help explain (e.g., dysfunction in coordination in activation/inhibition impedes both proper integration of networks that should be aligned and segregation of those that should not be).

This integration-segregation model of left hemisphere specialization is consistent with others that the left hemisphere is more analytic than global (e.g., see Babik [44]), although I would argue that the left hemisphere better integrates analysis and globality, as well, through its better transcallosal inhibition (and activation-inhibition coordination). In short, the activation-inhibition coordination model can retranslate other models in its terms, indicating its superordinate conceptual clarity.

Huber and Marsolek [45] reviewed research that the left hemisphere is associated with the approach motivation and the right hemisphere with the withdrawal motivation. For example, the left frontal hemisphere is specialized for approach-related processes (e.g., Fetterman et al. [46]) relative to the right hemisphere and its withdrawal processes (e.g., Pérez-Edgar et al. [47]; but see Garrison et al. [48]). Approach motivation is not described directly in terms of activation, but it clearly is, while withdrawal motivation is defined more directly in terms of inhibition (e.g., retreating from a threat or inhibiting one's responses, or both). It would make sense to examine the approach-withdrawal poles in terms of activation-inhibition coordination more directly. For example, adaptive, functional approach seems to require both activation and inhibition in coordination, while withdrawal requires inhibition alone for the most part.

Grimshaw and Carmel [49] presented a differential (asymmetric) inhibition model of the hemispheres based on the valence of perceived information. Greater right frontal lobe asymmetry (FA) is associated with better positive information inhibition, while greater left FA is associated with better negative information inhibition.

To test the hypothesis against the competing one that greater right FA should be associated generally with better inhibition skill (e.g., Aron et al. [50]), Schrammen et al. [51] studied right- and left-handers who were administered a tachistoscope task involving positive (friendly) and negative (angry) faces presented briefly, and so to the left or right (L, R) visual fields (VF) (and one hemisphere or the other). The task involved Go and NoGo responses, with more trials being Go ones. They measured false alarms on NoGo trials, used as an index of the degree of failure to inhibit. Furthermore, they examined the event-related potential (ERP) in reaction to the stimuli. Further, the authors extracted the alpha band (8–12 Hz frequency) data generated from EEG signals over the frontal lobe readings during the resting state. The averages might differ between left to right, with a right FA indexed by lower alpha band power in the right relative to the left frontal lobe readings, and vice versa. Stable, trait-like resting state right FA has been associated with multiple cognitive, affective, and personality factors, e.g., impulsivity [52], and with withdrawal-related tendencies and negative affectivity (developmentally [53])

Schrammen et al. [51] found complex results, and not all predictions were confirmed, but right handers did exhibit a stronger N170 ERP response over the right hemisphere and better response inhibition to LVF (right hemisphere)-presented stimuli. These results are consistent with the right hemisphere inhibition model.

However, other results indicated that the latter model is qualified by the valence (positive vs. negative faces) stimulus factor. According to the paper's abstract, the participants demonstrated better response inhibition to angry faces that were projected to the right hemisphere, and better response inhibition to friendly faces that were projected to the left hemisphere. The discussion repeated these results, but also qualified them later on as a trend instead of being significant. Inspection of the results section indicated that there was indeed a two-way ANOVA interaction, but more limited than the abstract indicates. Specifically, the VF X Valence two-way interaction indicated that RVF (left hemisphere) stimulus presentation yielded false alarm rates that were lower (indicating more inhibition) for the positive faces compared to the negative ones ($p < 0.01$), but the opposite pattern was only found at the level of $p < 0.07$. That is, for LVF (right hemisphere) stimulus presentation, the false alarm rates were equal for positive and negative faces, albeit they tended toward a difference in favor of lower rates for the negative faces.

Nevertheless, the Schrammen et al. [51] results can be taken to support the differential inhibition hypotheses of the left and right hemispheres. Moreover, consider that, in this study, the left hemisphere excelled in inhibition related to positive faces, which is consistent with the left hemisphere being related to positive emotions, unlike the right hemisphere. In this sense, the results are consistent with the activation-inhibition coordination model of the left hemisphere, which posits that the left hemisphere's positive emotion specialization reflects the more difficult dynamic of positive complex social interactions, generally, which would require advanced activation-inhibition coordination skills relative to the less refined inhibitory skills that would be associated with negative emotions.

Right Hemisphere Inhibition. This is also supported by findings showing that the right hemisphere is associated with simpler inhibitory functions, such as inhibition on its own (e.g., cortical and subcortical response inhibition; Maizey et al. [54]; also Bartolomeo & Malkinson [55]). Hartikainen [13] reviewed research pointing to superior right hemisphere inhibition. At the same time, the right hemisphere has dedicated attention-to-threat allocation skills, which might interfere with its inhibitory ones.

The right inferior frontal gyrus (rIFG) appears implicated in inhibitory control according to lesion studies (Choi & Cho [56]; also see Mayer et al. [57]). Not all research supports a right hemisphere advantage for outright stopping, though (e.g., Mancini & Mirabella [58]). These inconsistencies might speak to the overlooked notion that inhibitory functions are multifaceted in the brain and must involve a coordinated integration of both hemispheres in their activation as well as their inhibition for any one task, leading to task variations in this regard.

Infants. The right hemisphere is considered more expressive emotionally, including of its negative affectivity, and mothers tend to cradle their babies on the left side, which allows a reciprocal monitoring of the mother and baby of the left hemiface. This lateralized propensity in cradling allows better monitoring of the baby's emotionality and needs, according to Malatesta et al. [59]. The authors considered the left cradling bias partly heritable, and having an influence environmentally on the developing lateralization of the baby. From the present point of view, the hypothesis speaks to the bi-participant activation-inhibition inter-coordination required to reciprocally entrain adaptive dyadic interaction as well as lateralization.

Developmentally, the activation-inhibition coordination model of left hemisphere specialization has been hypothesized to be present neonatally [1]. That left hemisphere specialization develops neonatally along adult lines supports this conjecture. In this regard, Young and Gagnon [2] found that 2-day-olds turn more to the left to hear low-intensity music sounds coming from the midline behind them, and more to the right to hear low-intensity matched speech sounds. In a similar study, Morange-Majoux and Devouche [60] replicated these results, and expanded them using sucking bursts.

The latter underscores that inhibitory control is dynamically and environmentally influenced, and that activation-inhibition coordination is not an intrinsic function but a relationally co-regulated one. Similarly, Wu et al. [61] showed that infant maternal sensitivity played a moderating role in later preschool executive function/inhibitory control, at least for lower and higher levels of negative reactivity.

Early Frontal Lobe Valence. A critical question in the hemispheric specialization field relates to the exact nature of how the hemispheres are specialized for emotions, and whether superordinate concepts can explain the findings. EEG research indicates that more positive emotions, as well as the one of anger, are related to the left hemisphere (the frontal lobe, not the parietal) and other negative emotions to the right hemisphere. Workers have interpreted these respective left and right frontal lobe emotional specializations in terms of approach and withdrawal motivations (e.g., Harmon-Jones & Gable [62]).

These models require examination of the developmental research to better determine their origins. Developmentally, the model has been extended to the infancy period [53,63].

As described in Young [3], in this regard, Krzeczkowski et al. [64] found that, in socially avoidant mothers, the driver in 9-month-old EEG-measured FA at rest related to maternal rather than infant resting-state FA in two emotion-eliciting conditions (happy, fear). This indicates that the valence hypothesis of emotion and FA needs to consider the full social context.

Similarly, Diaz et al. [65] found a relationship among maternal insensitivity/intrusiveness, toddler negative affectivity, and hemispheric lateralization for affect in the frontal, lobes as measured by baseline EEG. Specifically, maternal sensitivity behavior at infants five months of age and also at 24 months of age were related to less affect negativity at the 2-year age mark, but only for infants whose baseline frontal EEG was asymmetric to the left. In contrast, maternal intrusivity at both ages was associated with later negative affect, but only for 5-month-olds who had shown right frontal EEG asymmetry.

Davis et al. [66] found atypical lateralization in the social gaze of preterm infants. They used eye-tracking of social and non-social stimuli presented to the left or right side of the stimuli presentation screen. Eye tracking measures were looking time related. The term and preterm born infants were examined when they were 8 to 10 months of age (with corrected age, the two groups were equal in months of age). The preterm infants expressed a reduced preference in viewing social stimuli in the left visual field, which indicates less social interest to stimuli on the left compared to controls, or less of a right hemisphere differential specialization for the function involved.

The results speak to the multiple ways that the typical process of hemispheric specialization develops but can go awry. Moreover, this development can be arrested early in life due to multiple factors, as the authors noted in their discussion, including from the stress associated with the preterm pregnancy and natality. These diverse influences on lateralization development can be termed biopsychosocial.

Beyond that, the question remains on the validity and inclusiveness of the valence model, the approach-withdrawal model, or any other model on the emotional and related differences empirically evident in hemispheric specialization. It is beyond the scope of the present paper to fully investigate this question. However, from a developmental perspective, the models seem valid, but still lack an overarching perspective, although the activation-inhibition coordination model might help in this regard. It points to the functionality of the emotions this way, toward maintaining the synchronized social interaction in dyads early in life, such as mother and baby, with the left hemisphere the seat of the advanced skill in this regard.

Early Laterality. In normal development, even the foetus can express a left hemisphere motor dominance for behaviors that fit the developmental level. In this case, in ultrasound research, Hepper [67] found that fetuses exhibited more right arm movements, and even early in the fetal period.

This illustrates that, at any age over the life cycle, astute researchers can capture laterality differences if they measure behavior that is at the cutting edge of the individual's developing skills. The tight palmar grasp of the neonate will be right-handed because that behavior is complex, but in later bimanual coordination grasping is subservient to fine motor manipulation, as in bimanual coordination, and so becomes the province of the left hand in that bimanual behavior. This illustrates the changing tapestry of laterality and handedness in development, so well described in the cascading model of Michel [68]. Multiple factors, including experience, affect laterality in behavior and lateralization in the brain.

In terms of the Michel's ([68], p. 8) description of the specializations of the right hand/left hemisphere and left hand/right hemisphere early in life at the motor level, his modeling is quite consistent with the present activation-inhibition coordination model. Specifically, he noted that the left hemisphere is specialized for "the production of precisely timed, serially ordered quick movement patterns". This skill contributes to the "articulation" of "sophisticated manual actions". The latter are found in "object manipulation, artifact construction, tool use, imitating actions, and communicative gestures and pantomiming". As for the specializations of the right hemisphere, they appear to offer "postural and contextual support for the manual actions produced by the left hemisphere". Michel presented the following analogous contrast for right and left arm skills—"Trajectory control and visual feedback for movement of the preferred right arm are processed more accurately, whereas positional control and proprioceptive feedback are processed more accurately with the nonpreferred left arm" (p. 8). Overall, Michel [68] could have concluded with a model much like the present activation-inhibition coordination one to describe the differences in left and right arm activity early in life.

Nonhuman Primates. As for chimpanzees, Hopkins et al. [69] demonstrated a population level right handedness for bimanual coordination in a tube task, although the side preference was reduced in wild compared to captive chimpanzees. The authors indicated that the groups differed by age and stress experience as much as captivity status. Hopkins et al. [70] generalized these findings to bonobos and gorillas, but not orangutans, given their different posture and locomotion status in their environment. Meguerditchian et al. [71] confirmed these manual specialization findings over different nonhuman primates, but found that gestural communication was uniformly a right hand skill. These results indicate that when posture is the driver of behavior, the left hand will be favored. But normally, for coordinated tasks, the right hand is favored, and gestural communication in nonhuman primates requires complex coordination as much as does human speech. To conclude, the activation-inhibition coordination model could be mapped onto these nonhuman primate findings, just as it could for early developmental findings, e.g., as described by Michel [68].

Evolution. Forrester et al. [72] presented an evolutionary model of laterization that considered basic sensory and motor biases as having evolved first, with later evolutionary acquisitions mapped onto (exapted) to the side of the brain that was consistent in function with the new skills. The generalized differential brain model in these regards suggests that the left hemisphere is specialized for structured or routine motor sequence skills and the right hemisphere for fight or flight behaviors. Respective examples for the left and right hemisphere specializations in modern humans include tool use and speech, representing left hemisphere motor-related skills, and emotion identity and face processing being better in the right hemisphere, which are extensions of underlying abilities in spotting danger and threat in the environment.

Note, that I take the description of left hemisphere motor skills as involving routines in several senses beyond one possible implication that it refers to simple tasks, which I presume is not the meaning. That is, according to the left hemisphere activation-inhibition coordination model, complex motor functions increase in skillfulness because of the said coordination in the left hemisphere. These motor skills possibly could maintain their locus in the left hemisphere as they become routinized. Or, the behavior requires constant adaptation to the ongoing context, and also to developmental changes, so that the left hemisphere remains their locus. Or, they might be shunted to the right hemisphere once they are less demanding in left hemisphere activation-inhibition coordination skills, especially when the left hemisphere skill set is required for new adaptations to context and the routinized behavior is less demanding simultaneously of those skills.

An open question relates to the back and forth nature of initiating a complex motor task and its ongoing improvement as it becomes routinized. Is the initial attempt too overwhelming for the left hemisphere's skill set and, therefore, it begins in an uncoordinated way through right hemisphere control? Then, the left hemisphere would chime in with its specializations to routinize the behavior as efforts continue. Or, does the left hemisphere take control of the behavior from its outset, given its skill set, and wade through to its successful routinization?

4.3. Interim Conclusion

In my own work, I carry the process of seeking differential foundational skills of the left and right hemispheres, both in the developmental and the evolutionary sense, one step further than other workers. For example, the model of the left hemisphere as being foundationally specialized for the coordination of activation and inhibition affords a common metric that relates different behavioral phenotypes, such as motor behavior specialized on the right side and also speech production. Furthermore, it allows for a more precise definition of the left hemisphere (right side) motor skills that are involved. On the one hand, they are more than routine, as just elaborated, because they could be complex, sophisticated, and subtle. On the other hand, they are more than structured, because they are dynamic, ongoing, adaptive to context, and seeking stability as they proceed without a definite structure throughout.

As for the right hemisphere, the fight or flight model is only part of the equation of the foundational specializations involved according to the activation-inhibition coordination model. That is, fight or flight (and freeze) reactions are rarely long relative to other behavior, and do not compare in the complexity of ongoing social interactions, which are presently conceived as examples of left hemisphere specializations generally because of the complexity and long duration of activation-inhibition coordination that seems required for their activity. That is, the fight-flight-freeze model of the right hemisphere applies well to it, but it is incomplete, and can be complemented by indicating that right hemisphere motor function includes less complex activation-inhibition coordinations, per Table 1, or outright inhibition (e.g., freeze), which is considered a primary inhibition-related right hemisphere function, as well.

One example that fits the present model relates to self-directed behavior in children compared to object-directed behavior. Forrester et al. [73] noted that the latter are left-hemisphere specialized, unlike the former, which are right-hemisphere specialized. This finding indicates that more complex as opposed to routine behaviors are left-hemisphere specialized, consistent with the present activation-inhibition coordination model. Forrester et al. [74] found similar results, but this time they opposed left-hemisphere object-directed behavior to a right hemisphere dominant animate-target behavior. The present model would refer to the animate target manual behavior as less complex than the social interaction across multiple modalities, which should be left-hemisphere governed, with the manually directed behavior accompanying it shunted to the right hemisphere as the complex interaction in other modalities proceeds. In support of my interpretation of these findings, the authors refer to the left hemisphere as being specialized for orchestrating hierarchical sequences of events. Rogers [75] considered the right hand skills more proactive and the left hand ones more reactive, which is consistent with the present approach, as well.

Another example that fits current conceptualization involves the left cradling bias, taken as an indication of right hemisphere emotional processing. It is shifted to the right by prejudice [59]. In terms of the present conceptualization, the accompanying normative left hemisphere specialization for complex social interaction as afforded by the normative left hemisphere's specialization for activation-inhibition coordination is no longer recruited in the case of prejudice, thereby diminishing the shunting to the right hemisphere of less complex facial perception/processing (as afforded by the left cradling bias) in order to free up the left hemisphere for more complex social processing/activation-inhibition coordination. Similar explanations apply to the association of reduced left cradling bias with more maternal depression (e.g., Malatesta et al. [76]; Pileggi et al. [77])—the latter would serve to reduce the impetus for ongoing social interaction with the baby (and left hemisphere activation-inhibition coordination skills), thereby reducing the shunting to the right hemisphere of less complex social behavior, as in face perception/processing occasioned by left cradling bias. As well, its reduced association with autism spectrum disorder (e.g., Herdien et al. [12]; Forrester et al. [72]; Pileggi et al. [78]) is not unexpected from the present perspective.

The literature and its review have been far-ranging, much like the activation-inhibition coordination model to which it is addressed. The review analyzes literature related generically to the question and then specifically to the concept that the left hemisphere is specialized for this advanced skill. It finishes by examining developmental and evolutionary work, showing that the model applies to these different scales, as well, in terms of lateralization of brain and behavior.

5. Discussion

Recent conceptualization and research is supporting more directly the concept that activation-inhibition coordination is a common explanatory underpinning mechanism across the multiple scales from neuron to brain to behavior. Moreover, the research and concepts are supporting that the left hemisphere is specialized for the activation-inhibition coordination function. The concept can also help explain how functionality at these scales can go awry and contribute to disordered activity, including in neurological and behavioral/mental disorder. There are signs of specificity in the underlying activation-inhibition dyscoordination dynamic with respect to different neurological/behavioral-mental disorders.

A good test for the validity of the concept would be to take another lateralized behavior and examine its structure according to its fit with the activation-inhibition coordination model. In this regard, role differentiated bimanual manipulation can be considered a key evolutionary acquisition, and it develops early in a lateralized way [79]. By 1 year of age, for example, infants are capable of removing one object inside another, by stabilizing the object with the less skilled hand and using the skilled one for retrieval. By 2 years of age, toddlers can unzip a zipper with an equivalent role differentiation. The behavior is liable to lateralization, and reflects the early development of the left hemisphere for fine motor skills. The developmental model that best explains the lateralization is referred to as the cascade model, for example, the lateralization begins with the head position in the womb, which has experiential transfer effects to other developing behavior [68]. For nonhuman primates, an equivalent task that is used involves the coordinated bimanual tube task [80].

In these bimanual role-differentiated coordinated skill behaviors, the stabilizing hand needs to be positioned on the object (e.g., tube), and then the manipulation to obtain the target item can be attempted. Each phase of the task requires activation-inhibition coordination, as generically represented in Figure 1. Stabilizing requires inhibition of interference to properly activate the sequences to reach, grasp, adjust, etc., which also includes creating postural stability, all of which serve to prepare the eventual opposite-hand manipulation. The behavior of manipulating is even more refined in this regard, which explains why the left hemisphere (right hand) is involved for the behavior, thereby relegating the stabilizing function to the left hand. Specifically, manipulation involved a refined, fast-moving synchronization of fingers, the wrist, the full arm, and the shoulder, while coordinating with looking and postural stability. That is, for the apex function of activation-inhibition coordination posited as a left hemisphere function, when task and behavior demands require this level of sophistication in the manual behavior, such as in the role differentiation under discussion, it will be normative for the right hand (left hemisphere) to undertake the more complex role.

Thus, there are several levels of coordination in the hemispheres that take place in this example. First, the left hemisphere coordinates the particular sequences for the behavior while controlling interferences. Second, it coordinates the right hemisphere (left hand) and its skills toward task and goal adaptive success. The example illustrates how behaviors can be decomposed into units that fit the activation-inhibition coordination hypothesis of left hemisphere specialization. Kinematic research should be undertaken to support this analysis of left vs. right hemispheric specialization, and the role of inhibition therein. Young developed the hypothesis of left hemisphere specialization of activation-inhibition coordination by analyzing the simpler reaching of 1-month-olds. There is no contradiction here, because, as Nelson [79] pointed out, one measures laterality with tasks that fit the age of the child.

In this regard, proper testing of the activation-inhibition coordination model of left hemisphere specialization requires programmatic research. It will contribute to reframing the function of the neuron, cortical networks, brain in general, and the complex individual and social behavior of all species in its form.

6. Conclusions

The paper has presented a comprehensive description and defense of the activation-inhibition coordination model. It was developed to help explain the better coordinated reaching behavior of the right hand in 1-month-olds [2], but also has currency for understanding left hemisphere specialization specifically and neuronal/brain and behavior, generally. The model makes specific predictions, aside from reviewing other work in its terms. It gives a common mechanism for understanding behavior and its causation across multiple scales, including developmentally and evolutionarily. It has practical implications in that it could help explain brain and behavior disturbances according to its terms, perhaps leading to novel conceptions of intervention and treatment.

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