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Mini-Review

Allocation of attention and higher-level representations as therapeutic tools to assist people with neurological conditions: A proposal that integrates research and practice

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ABSTRACT

The present perspective piece elaborates recent extensions of a framework that focuses on motor and cognitive processes. The key findings underlying the proposed framework come from research on bimanual actions. It is proposed that general principles emerging from this work are potentially applicable to a broad range of motor and cognitive skills. The present paper is an attempt to outline the framework and provide a context to encourage discussion and generation of ideas across fields, with the hope of bringing together and translating basic research findings into efficacious therapies.

KEYWORDS: bimanual actions, coordination, higher-order representations, conceptual, perceptual.

INTRODUCTION

One could argue that the most-used system in human voluntary actions is the bimanual system, which involves the brain's representation, planning, control, and feedback processes associated with actions of our right and left hands [1]. The present mini-review presents a perspective on a specific strand of research in the domain of bimanual actions which focuses on the manner in which higher-level representations may be used to overcome lower-level forms of bimanual interference. The framework and supporting evidence are elaborated with an aim of generating discussion and useful research approaches toward the development of efficacious therapeutic methods to assist people with neurological conditions. The paper is organised according to the following outline:

1. Brief context of the research program in terms of techniques and key foci
2. Historical context for development of the proposed framework
3. Elaborated model of brain organisation underlying the framework
4. A working model of focused attention for action
5. Some examples from other research domains which are consistent with the proposed framework
6. Suggestions and hints for translating research into therapeutic avenues

1. Brief context of the research program in terms of techniques and key foci

Laboratory-based research on bimanual actions led to the development of the present framework. Like all models used to guide research, this framework requires rigorous experimental investigation. Toward that aim, the present author's laboratory currently employs multimodal methods of functional magnetic resonance imaging (fMRI), electroencephalography (EEG), and forms of structural MRI including diffusion tensor imaging (DTI), in conjunction with

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a range of behavioural techniques [see https://web.psy.otago.ac.nz/liz_site/home.html; https://www.otago.ac.nz/psychology/staff/elizabethfranz.html].

This research requires considerable reading and rereading of empirical papers and intensive learning of cutting edge techniques; it also requires communication with neurologists, and working with numerous participants from the local community and all over the world. Experimental methods are applied to learn about the neurologically normal (intact) brain and, by comparison, how identifiable functions indexed by dependent variables differ (from normal) in the brains of individuals afflicted by neurological conditions or diseases. This experience has provided researchers in the present research program the privilege of working with a large range of individuals with either relatively common disorders/diseases such as Parkinson's disease, Essential tremor, and forms of dementia, and also those with less common conditions such as congenital mirror movements, callosal agenesis, rare effects of stroke such as alien hand syndrome, and post-surgical callosotomy. Review of portions of the work leading up to the development of this framework can be found in [1-4].

Ideas which date back to the nascent insights of neurologist John Hughlings Jackson (JHJ) formed the foundation of a model of brain organisation that the present framework has expanded and elaborated on. The emergent framework captures a large range of behavioural findings related to the bimanual action system (reviewed in [3-5]). The suggestion has also been put forth that the framework helps to reconcile a mix of findings from neuroimaging studies across the fields of neuroscience, psychology, and neurology [6], as well as some curious collections of symptoms seen in some psychiatric disorders [7].

2. Historical context for development of the proposed framework

According to the early writings of John Hughlings Jackson (reviewed in [6]), the brain is fundamentally a sensorimotor machine comprised of basic (lower-level) sensorimotor networks on which higher levels of representation and re-representation have evolved through adaptations with the environment. Revitalization of the JHJ framework was stimulated about a decade ago by a research finding on bimanual actions [5]. That study set out to test the idea that the brain's so-called higher levels of representation (those which are conceptual and/or perceptual) will override lower levels of representation (those which are sensorimotor) that often result in interference effects in planning processes of the two hands; thus, the higher-order representations, once attended and learned, will guide actions. Franz and McCormick defined lower-level as the basic forms of sensorimotor interactions which produce 'bimanual interference' which often is referred to as 'spatial coupling' [1, 8, 9]. Spatial coupling can actually come in many forms; relatively complex, and simple. One example is when circle shapes are to be drawn by one hand, and simultaneously, line shapes are to be drawn by the other hand. Rather than each hand drawing its assigned shape, the outcome is typically some form of elliptical shapes or combinations of circles and lines [8-10]. Some forms of spatial coupling occur through interactions between cerebral hemispheres which are mediated by the corpus callosum [11]. A higher-level form of spatial coupling might also occur, and can be indirectly observed when sensorimotor systems are not intact (e.g., in the case of a phantom limb following amputation; [10]).

A task in which simple forms of spatial coupling have been investigated is bimanual movements in which the two hands must reach and touch target objects that are either the same distance away from the body (congruent), or two different distances away (incongruent; i.e., one hand is assigned to reach to a far target and the other, a near target). In incongruent trials, rather than the two hands producing the movement amplitudes that were assigned, accommodation occurs between the hands. Furthermore, although the two hands tend to begin their movements at the same time, those measures of reaction time (which are used experimentally to index 'planning time') tend to be longer when the movement demands are incongruent compared to congruent ([5]; see also [12]).

Franz & McCormick [5] tested specifically whether higher-level perceptual representations and/or higher-level conceptual representations would reduce interference effects that occur in incongruent trials (see Figure 1). The perceptual

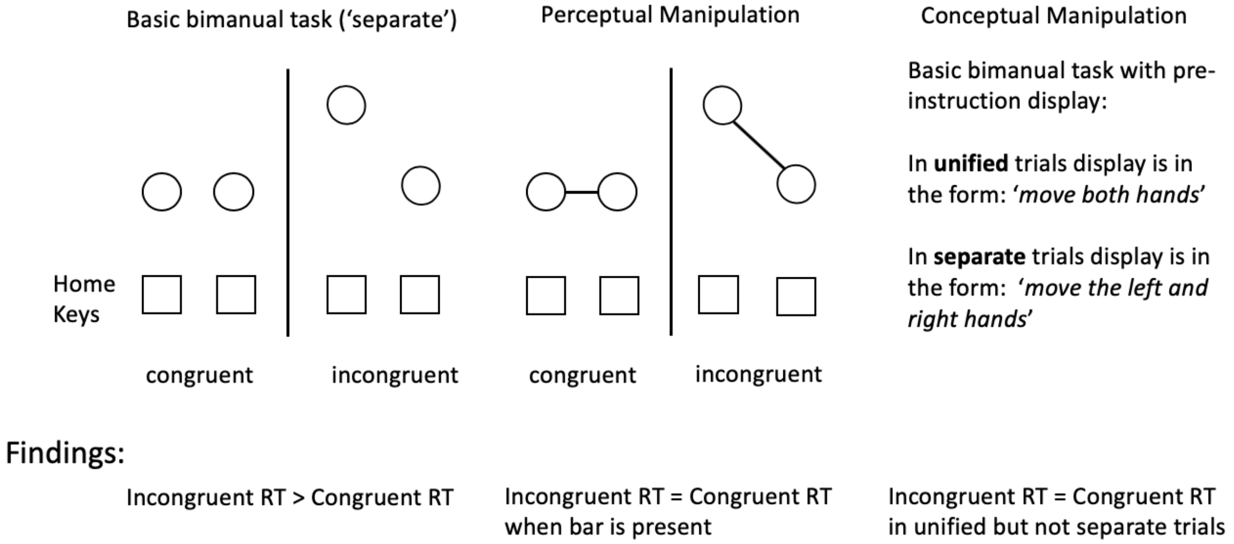

Figure 1. Examples depicting key experimental manipulations used in Franz and McCormick [5]. RT = Reaction Time. On each example trial, squares represent the left and right starting points (home keys). Circles represent the target objects that the left and right hands are required to reach. One example of a congruent trial and one example of an incongruent trial are shown here to illustrate each experimental condition. When a bimanual task is unified for the two hands, higher-level representations are thought to override lower-level representations that typically would produce interference. In this example, unified conditions are manipulated either perceptually or conceptually, resulting in reaction times that are approximately equal for congruent and incongruent trials. In the basic task in which no 'unifying' representations are present (i.e., 'separate'), reaction times for incongruent movements are on average longer than (>) reaction times of congruent movements [Modified from 5: see text for further details].

manipulation was to display the two targets with a connecting bar between them (rather than as separate targets as in the basic task paradigm). The conceptual manipulation was to employ subtly different word phrases as instructions on trials so that phrases such as 'move both hands' comprised one condition (referred to as unified actions) and phrases such as 'move the left and right hands' formed trials in another condition (referred to as separate actions). The aim was to create those trial conditions so that a single unified action plan would be evoked (in the brain) during planning of trials with instructions using the word 'both', whereas, two distinct action plans would be evoked in trials using instructions implying two separate/distinct movements. In sum, findings using the perceptual manipulation were similar to those using the conceptual manipulation. Reaction times of incongruent and congruent movements were similarly short when the tasks evoked a unified action plan (see Figure 1) [5]. Although that example was not applied to neurological patients, it provided initial evidence that higher levels of control can be used to override lower-levels, leading to development of the present framework.

As stated above, the bimanual action domain has been useful in providing initial experimental evidence consistent with the idea that higher levels of representation can override lower-levels. However, the bimanual literature did not provide a model framework for such findings. In a very enlightening exercise, reading the literature 'backward in time' about 150 years led to an exciting rediscovery of the writings of John Hughlings Jackson scattered across a number of medical journals. JHJ used the terms 'representation' and 're-representation' in describing the manner in which layers of higher-level brain networks are embedded upon lower levels of what is fundamentally a sensorimotor machine (reviewed in [6]). This idea of JHJ forms the basis of an integrated model of brain organisation of the bimanual action system [3-7] that the present author proposes might be applicable to a range of other skills.

In the days of JHJ, no neuroimaging techniques had yet been developed. His insights were based on careful observations of randomly presented patients who sought advice upon experiencing neurological problems across a broad range. JHJ's three-level system had the motor cortex at its highest level. The more recent elaboration of that model begins with the motor cortex and associated circuits at its lowest level, with higher levels embedded upon those lower levels [3].

3. Elaborated model of brain organisation underlying the proposed framework

In the elaborated model, the motor cortex and accompanying sensory areas of the brain are obvious candidates of inclusion in a basic sensorimotor network. Furthermore, research has strongly suggested that the basal ganglia, a subcortical complex of interconnected nuclei, contribute to functions of motor behaviour, emotions, and cognition [13]. Notably, the basal ganglia operate as an integral component of a large number of parallel basal-ganglia-thalamo-cortical circuits, given that cortical input from widespread brain areas converges on the input nucleus (the striatum) of the basal ganglia; following processes through direct and indirect circuits, projections ascend *via* thalamic nuclei [14] back to cortical areas ([13-15]; reviewed in [2, 4]). Those parallel circuits fit nicely into a lower-level (i.e. sensorimotor) to higher-level (i.e., higher cognitive functions) framework. Widespread functions, therefore, are thought to rely on basal ganglia-thalamo-cortical circuits of which some are basic sensorimotor circuits (often referred to as 'motor circuit'), and other parallel circuits are involved in higher-order functions (perceptual/conceptual). While the examples so far pertain to motor actions, the circuit interplay would differ for other types of skills, i.e., other cognitive skills.

4. A working model of focused attention for action

In the development of the present model, a further question was addressed: How does brain activity 'shift' between the different circuits comprising the parallel architecture just described? It is proposed that a key component involves the concept of 'focused attention' [4]. Again using the basal ganglia as an example, the complex of nuclei and associated circuits has been conceptualised as a network in which a key function involves focused selection of desired actions and another is inhibition of potentially competing information and prepotent actions [2, 4, 15]. Accordingly, 'focused attention' is construed in the present framework as having a function in the shifting of brain activity from one circuit to another. This also fits nicely with the notion that higher-level circuits might be enlisted (for a particular task) thereby resulting in focused attention on those selected circuits while attention to lower-level circuits is reduced or eliminated [4]. Thus, according to the present view, a shift in brain activity might be akin to a shift in attention, as though attention 'moves' depending on the task, situation, and context [4]. This view stems from related work on attentional shifting in people with Parkinson's disease [16-18]. Notably there are likely to be unconscious forms of attention switching as well as more conscious forms (see examples in [4].

When considering the manner in which the brain changes through adaptive learning, a relatable conceptual example is learning the piano, which involves first learning the simple sensorimotor elements in a feedback-guided manner. That feedback likely involves primarily vision and proprioception, but also auditory feedback associated with hearing the outcome of motor actions (i.e., the notes). Once sensorimotor elements are learned, the performer's attention might shift to higher-level representations such as the whole melody [3, 4, 19]. It is as though attention has 'moved' from the lower-level elements to higher ones as proficiency increases. Indeed, that elusive process referred to as attention seems to have the properties of 'moving' in a manner akin to activation of an interplay of different neural circuits [4]. The so-called 'movement' of attention is a critical part of the present model and also opens the door to numerous possibilities for therapeutic treatments given that attention can be guided volitionally, i.e., through learning. Because motor learning is perceptually based, and perceptual representations can be readily used to guide performance [20], the framework also provides a tool for guiding methods of learning, as it is possible to instruct people to attend to different forms of information in the context of a task.

The examples above relate nicely to recent research using sonification, in which auditory concurrent feedback is employed during learning of a task (recently also tested using bimanual methods; [21]). This method requires less transformation than forms of visual feedback and therefore might be a useful alternative method for learning. The technique aims to enhance temporal control (i.e., timing) of movements/actions using sound, with different notes occurring when elements of the movement task are produced by a participant so that a higher-order ‘melody’ can be used as concurrent feedback (details of technique and related studies reviewed in [21]). While the examples cited so far come from relatively recent research in neurologically normal participants, they seem to offer potential for exploring methods to facilitate learning of skills (or re-learning of skills) in individuals with neurological conditions. This area of research-informed-therapy is wide open.

5. Some examples from other research domains which are consistent with the proposed framework

How might one go about testing within the framework described, with aims toward eventual therapeutic/strategic treatments to assist individuals in skilled behaviour? To pave such a path, it might be wise to relate the framework to some examples from neurological conditions that are not diseases as such, but which affect skilled behaviours that are not necessarily bimanual. In particular, one might consider disorders that are not known to be degenerative, and likely would benefit from strategic therapeutic treatments of the type that enable for an overriding of the unwanted sensorimotor symptoms that potentially interfere with skill performance. One might consider developmental stuttering [22-26], which is not thought of as a disease although it is a more common disorder than might be assumed (prevalence estimated to be about 1% of adults; [27]). Forms of neurogenic (acquired) stuttering have been linked to damage involving nuclei of the basal ganglia [26, 28, 29] and also the supplementary motor area (SMA; [30]) and left ventrolateral (VL) thalamus [29]. Studies on the neural correlates of developmental stuttering are becoming increasingly common [31], with some research suggesting involvement of the basal ganglia and basic sensorimotor circuits among other brain areas [26, 32]. Neuroimaging studies, using speech and non-speech tasks which also include perception of speech, have demonstrated abnormal activity in auditory-motor structures in people who stutter [32]. Evidence based on cerebral blood flow (positron emission tomography; PET) techniques [33] and more recently fMRI [32] also has suggested that the brains of stutterers might differ more generally from those of people who do not stutter. Specifically, group differences occur even on non-speech tasks across numerous brain areas on whole brain analysis (in addition to more specific areas assessed through analyses on Regions of Interest; ROIs). Thus, it is important to take into account global differences which might not be as amenable to learning/therapy-related improvements. Diffusion tensor imaging (DTI), which assesses the integrity of white matter tracts, has revealed abnormalities (in comparison to controls) in the tracts connecting auditory and sensorimotor regions of the left hemisphere of stutterers. Abnormal morphology in brain sulci and/or cerebral asymmetry has also been reported [33]. While not an exhaustive list of neural correlates, this brief coverage of some of the research evidence points to what the present framework refers to as lower-level sensorimotor structures as playing a role.

Behavioural studies have shown that providing external cues using a metronome pacing signal reduces deficits in developmental stuttering [22]. Use of external cues likely implicates different circuits than use of internal cues (those related to one’s own proprioception). Internal cues have been linked with circuits involving the basal ganglia, whereas external cues have been linked with circuits involving the cerebellum [34, 35]. This melds well with findings relating to basal ganglia operations in the learning of actions [36] particularly given that more automated actions (e.g., speech) likely involve internal cues (see [4] for review, and [26] for review of the critical role of dopamine).

In considering possible higher-level representations, two key effects related to stuttering come to mind.

One is the so-called 'rhythm effect', which involves use of an external cue such as a metronome to pace speech, and the other is to have a person who stutters attempt to sing words (rather than speak them). Both are known to reduce speech dysfluencies in stutterers. As suggested by Alm [26], "It seems reasonable to suppose that during singing, the internal representation of rhythm provides internal timing cues for the initiation of each syllable in a similar way as a metronome provides external timing cues. If this assumption is correct, the dramatic effect of singing to eliminate stuttering in most persons who stutter can be viewed as an indication of dysfunctional timing cues in stuttered speech." ([26] p. 330). Whatever the precise reason for the improvements observed in speech fluency, both examples seem consistent with the notion that higher-level representations can be used to override sensorimotor effects at lower levels.

6. Suggestions and hints for translating research into therapeutic avenues

Research on basic neural mechanisms of stuttering, coupled with investigations into the effects of different forms of feedback and higher-level representations in reducing stuttering symptoms, ties nicely with the same conceptual framework that has guided the research on bimanual actions discussed above. Thus, the neural and behavioral research seems to be providing strong clues for developing avenues toward therapeutic methods aimed to assist people in using higher-level representations to overcome/override the dysfluencies characteristic of the disorder, stuttering. Research-based information will also inform models that might attempt to use sonification or other forms of feedback. It is also important to point out that potential effects of effort (in particular, differences in effort across groups such as those who stutter versus controls who do not stutter) are also not completely understood. Those issues are ripe for further investigation.

An underlying assumption in the present framework is that action representations are dynamic as is the pattern of activity of involved neural circuits during processing in different contexts of performance and learning. Perhaps the most important point to emphasise is that researchers and clinicians acknowledge that the brain is a flexible, dynamic, system which changes not only as a result of damage and/or progression of disease, but also as a function of practice and learning. It is critical that we leave open the possibility that strategic attempts toward therapeutic treatment might need to change with such learning. Even simple changes such as using one type of cue instead of another might result in large differences in performance (and possibly also, amelioration of symptoms given higher-order levels overriding lower levels). Furthermore, specificity of feedback might be crucial, given that intrinsic feedback might be more at play under some conditions and levels of learning than extrinsic forms, or vice versa [37].

CONCLUSION

As a summary of the above, and in the hope of arriving at avenues for development of further therapeutic methods to assist people, the following tips might be helpful:

- The specific phenotype of a disorder/condition must be assessed/defined where possible, in addition to whether and how it changes in an individual with time, learning, and other factors. This is particularly difficult given that, while collections of symptoms tend to form different classes of disorders (or spectra), no two participants (or patients) are actually identical. Specific methods of phenotyping are becoming more common for neurological disorders, e.g., differentiating Parkinson's tremor from Essential tremor [38]; classifying phenotypes of mirror movements [39].
- Variance across individuals is inevitable, and attempting to develop treatments to accommodate those differences requires great effort and often many years' experience. In research studies, it is often critical to recruit as large as possible sample sizes and to assess effects with statistical methods while also correcting for multiple comparisons where appropriate. Cherry-picking of specific examples is not recommended; however, if the condition is extremely rare (such as a case study), a single-case statistic can be performed in the first instance and this involves a large control

(i.e., 'normal') group for comparison. As an example, for rare cases a basic test is to assess where on the control sample distribution each single case falls (where the estimated population mean and variance come from the sample control distribution; e.g., [39]).

- Discussion across experts is crucial in facilitating interactions and arriving at useful methods efficaciously. This includes discussion across researchers and clinicians, something quite prevalent in some circles but not so in others, particularly in instances where researchers and neurologists are working in relative isolation. The extent to which clinicians can refer to published research in development of therapeutic methods, and the extent to which researchers are familiar with the symptoms of neurological conditions/disorders based on first-hand evidence of neurologists, the better.
- Just as it is important for a new learner (of any type) to use task goals to guide behaviour and learn to attend to relevant feedback, the context of task goals is also important to carefully consider. Attention is dynamic and we cannot take for granted that we know what a person is focusing attention on. As earlier findings suggest, even the words used to instruct a task can change behaviour ([5]; Figure 1); thus it is important to carefully instruct participants/patients and if possible, to do so in the context of specific task goals that they are to try to attend to. In sum, it is crucially important to remember, as researchers as well as practitioners instructing on specific therapies, that even task goals can be ambiguous and must be described carefully [40].
- Logging of behaviour is critical, and in the busy working life of most people, it is often difficult to do. In longitudinal studies, some research groups are able to log behavioural points in each participant over time, due to having a research team dedicated to such tasks. However, clinicians might find that time is rather limited with each patient, due to the many other demands of their work. Having a patient log periodically his/her subjective experiences in using a particular therapy can be helpful. In a recent case, the author's research team was contacted by a lovely woman through email asking for assistance in alleviating pain in her phantom limb following surgery, as she had been in chronic pain for quite some time. Applying a mirror-reflection technique that stemmed from insights based on observations of people with phantom limb movement [11] seemed worthwhile to try. The woman logged her experiences in using the mirror technique, and the research team was able to liaise with her caretakers to further assist. It is the hope of the present author that essential roles provided by volunteers in the community (such as those who performed the much-needed links between patient and researcher in the case just described) will eventually become paid career paths.

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CONFLICT OF INTEREST STATEMENT

There are no conflicts of interest.

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