ZING PERFORMANCE

The Science

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Executive Summary

Zing Performance has the potential to be a world leading platform for self development, with an innovative approach, scalable implementation, and a range of application domains. The key overall requirement is a world leading scientific 'core' that permeates and strengthens all aspects, providing synergy between the rationale, the implementation and the user experience. I first situate Zing Performance within the general ‘coordinative exercise’ (CE) intervention framework, thereby facilitating converging evidence of efficacy from recent CE studies both for memory and balance. Taken together with published evaluations of Zing Performance effectiveness for declarative and procedural processing, I consider these provide solid evidence of effectiveness.

Turning to the scientific underpinnings of Zing Performance, I then identify the unique feature of the Zing Performance programme as ‘natural vestibular stimulation’ (NVS) which floods the entire brain and body with activation. Next, basing my analyses on recent developments in the cognitive neuroscience of the functional connectivity and neural plasticity of brain networks, I analyze the key 'neural drivers' of change during NVS, identifying three classes: <u>neuroplasticity</u> enhancement (NPE) **-** the brain is primed to adapt; <u>network co-activation</u> – almost all the brain networks are activated at the same time; and <u>stochastic challenge</u> **-** the brain is repeatedly confronted with things it can't do, forcing it to try to change. This means that the claimed objectives of improvement in attention, memory and coordination can be firmly grounded in best current scientific knowledge. I then develop a series of ‘rainforest’ analogies for NPE which may elucidate the underlying mechanisms.

The analysis identifies the drivers of change, suggesting a two mechanism approach: first a ‘baseline progression’ programme, maintaining NP readiness (corresponding to the majority of the Zing Performance activities); and, second, a series of ‘Plasticity Packages’ (PP) providing both a challenge and a suite of activities designed to achieve a specific outcome.

Content

1 BACKGROUND

1.1 THE VESTIBULAR SYSTEM

The concept of 'healthy mind in healthy body' was of course an essential belief of the Victorians. After a century of suppression, this belief is now fully re-established, with the benefits of exercise for all aspects of physical and mental health and for all age groups now fully established using modern cognitive neuroscience techniques. There is extensive evidence that exercise has beneficial effects for people of all ages, and appears to improve not only physical fitness but also mental fitness, and even stimulates the growth of new brain neurons and connections (Hillman, Erickson, & Kramer, 2008).

A recent discovery has been the differential effects of cardiovascular exercise and coordinative exercise (such as Tai Chi or Zing Performance). There is strong evidence that exercise can potentiate the brain for new learning, with coordinative balance exercises leading to neural growth in the hippocampus (Niemann, Godde, & Voelcker-Rehage, 2014)- a core structure for explicit learning and memory, and specifically spatial memory - and also in the cerebellar-cortical loop (Burciu et al., 2013) - a core network for implicit learning and coordination.

These benefits are somewhat counterintuitive, especially for scientists schooled in the now outdated belief that physical, mental and emotional health are separable. Strikingly, the benefits of coordinative balance exercises are now strongly established. To take six recent examples,

(i) Changes in memory, spatial cognition and balance following 12 weeks balance training with healthy adults (Rogge et al., 2017)

"*In the present study, we tested the hypothesis that a demanding balance training program improves memory and spatial cognition. Forty healthy participants aged 19-65 years were randomly assigned to either a balance or relaxation training intervention. Each group exercised twice a week for a total of 12 weeks. Pre-and posttests assessed balance performance, cardiorespiratory fitness, memory, spatial cognition, and executive functions. Only the balance group significantly increased in balance performance from pre-to posttest, while cardiorespiratory fitness remained unchanged in both groups. Moreover, the balance group significantly improved in memory and spatial cognition. Effects on executive functions were not observed. These results suggest that balance training is capable of improving particularly memory and spatial cognition. Therefore, an increase in cardiorespiratory fitness does not seem to be necessary to induce beneficial effects of physical exercise on cognition. It might be speculated that stimulating the vestibular system during balance training induces changes of the hippocampus and parietal cortex possibly via direct pathways between the vestibular system and these brain regions."* .

(ii) Brain changes following 1 hour of balance training with healthy adults (Taubert, Mehnert, Pleger, & Villringer, 2016)

"We used MRI to test the hypothesis of immediate and specific training-induced alterations in motor cortical gray matter in humans. We found localized increases in motor cortical thickness after 1 h of practice in a complex balancing task. These changes were specific to motor cortical effector representations primarily responsible for balance control in our task (lower limb and trunk) and these effects could be confirmed in a replication study. Cortical thickness changes (i) linearly increased across the training session, (ii) occurred independent of alterations in resting cerebral blood flow and (iii) were not triggered by repetitive use of the lower limbs. Our findings show that motor learning triggers rapid and specific gray matter changes in M1."

(iii) Balance and gait training with older adults (Li, Bherer, Mirelman, Maidan, & Hausdorff, 2018)

"Finally, we discuss recent work on focused cognitive training, exercise and multimodal training of older adults and their effects on postural and gait outcomes. In keeping with the principle of neural overlap, the available cognitive training research suggests that targeting processes such as dividing attention and inhibition lead to improved balance and gait in older adults."

(iv) Change in physical, cognitive and educational attainment in junior school children with literacy problems following 6 months complex balance training (Reynolds, Nicolson, & Hambly, 2003)

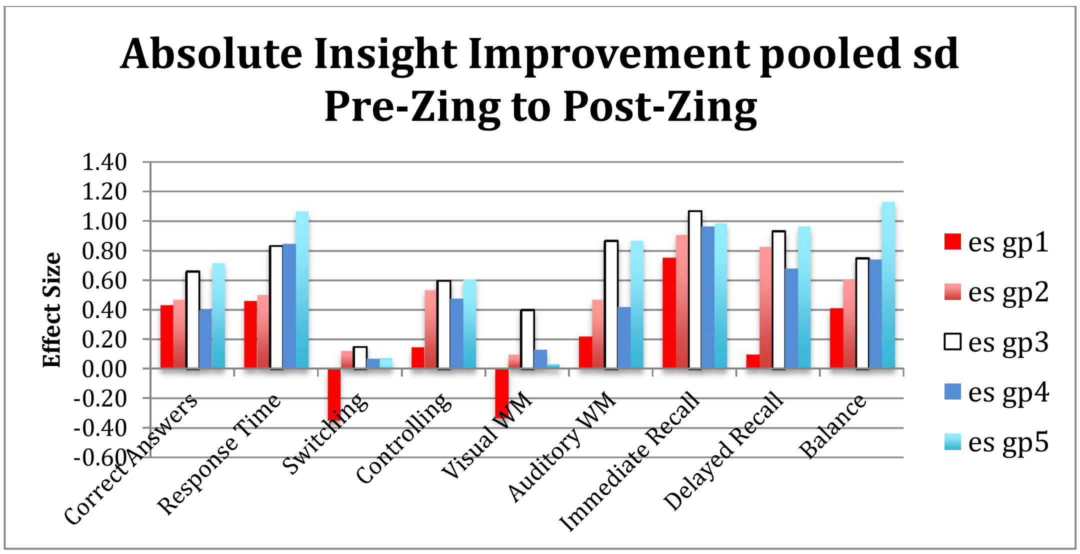
"Pupils in three years of a Warwickshire junior school were screened for risk of literacy difficulty using the Dyslexia Screening Test (DST). The 35 children scoring 0.4 or over on the DST were divided randomly into two groups matched for age and DST score. ... Both groups received the same treatment at school but the intervention group used the DDAT exercise programme daily at home. ... It is concluded that, in addition to its direct effects on balance, dexterity and eye movement control, the benefits of the DDAT exercise treatment transferred significantly to cognitive skills underlying literacy, to the reading process, and to standardized national literacy attainment tests".

(v) Changes in memory, spatial cognition and balance following 6 months Zing Performance balance training with older adults (Gallant & Nicolson, 2017).

"All participants undertook an initial series of pre-tests, and then an identical set of post-tests around three months later. The test battery comprised five suites of tests designed to evaluate cognitive-sensori-motor-affective functions, including Physical Coordination, Memory, Language Dexterity, Fluid Thinking and Affect. The intervention group showed significant pre- to post improvements in 12 of the 18 tests, whereas the controls improved significantly on one only. Furthermore, the intervention group improved significantly more than the no-intervention group on three tests - Balance, Peg Assembly and Delayed Picture Recall. Frequency of intervention use correlated significantly with the improvement in balance and in peg-moving speed. It is concluded that an internet-based balance and coordination programme for older adults can lead to benefits in balance, coordination and declarative memory."

(vi) Changes in memory, spatial cognition and balance following 200 days Zing Performance balance training as a function of participation frequency. Internal data on Zing Performance (2018)

The maximum number of sessions was 800, groups 1-5 undertook 1-199; 200-449; 450-599; 600-669 and 670-800 sessions respectively. A total of 365 participants was included.



Overall, therefore, although the benefits of Natural Vestibular Stimulation (NVS) were until recently considered to be unproven, recent research studies, from many laboratories and with the full range of ages for participants, have demonstrated clear and distinctive benefits using a range of NVS interventions (thereby providing converging support for the evidence on Zing Performance benefits).

1.2 WHY ARE THERE BENEFITS OF NATURAL VESTIBULAR STIMULATION?

For many years the focus of cognitive neuroscience research was on the cerebral cortex, but as brain imaging became more sophisticated, it became clear that sub-cortical structures including the basal ganglia and the cerebellum were involved in almost all mental activities. Furthermore, the development of methods for identifying functional connectivity through imaging, has led to the emergence of the vestibular system as a major source of inputs to the brain. A schematic description of the multiple circuits involved in the vestibular system is shown in figure 1. It may be seen that there are four linked circuits, three to the hippocampus, and one to the cerebellum. It should be stressed that the hippocampus and the cerebellum are the major 'hubs' for the two major types of brain circuit, with the hippocampus core for all 'declarative' processing (involving conscious awareness) and the cerebellum core for all 'procedural' processing (without conscious awareness).

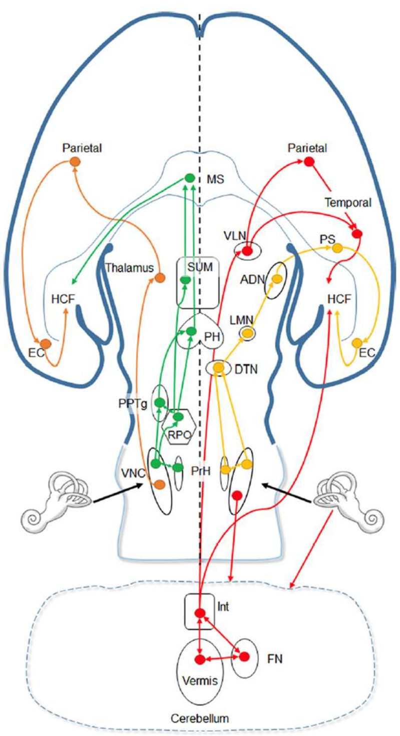


Fig. 1. Proposed pathways from the peripheral vestibular organs to the hippocampus on a diagram of a horizontally sliced rat brain. Thalamocortical pathway (orange); theta-generating pathway (green); cerebellocortical pathway (red); head direction pathway (yellow). ADN, anterior dorsal nucleus; DTN, dorsal tegmental nucleus; EC, entorhinal cortex; FN, fastigial nuclei; HCF, hippocampal formation; Int, interpositus nuclei; LMN, lateral mammillary nucleus; MS, medial septum; Parietal, parietal cortex; PH, posterior hypothalamus; PrH, prepositus hypoglossi; PPTg, pedunculopontine tegmental nucleus; PS, postsubiculum; RPO, reticularis pontis oralis; SUM, supramammillary bodies; Temporal, temporal cortex; VLN, ventral lateral nucleus of the thalamus; VNC, vestibular nuclei. Reproduced from Aitken et al. (2017b) with permission.

In short, natural stimulation of the vestibular system leads to excitation in several major brain circuits, and in addition many directly related and additional systems.

What does seem now to have been established regarding the vestibular system, is first that is it directly involved with the sensorimotor systems for balance in the brain, and reflexes such as the vestibular ocular reflex for maintaining the eyes steady well the while the head moves or accelerates. Most recently however it has become clear that the vestibular system is very closely linked to the major declarative circuitry including the hippocampus.

1.3 How can we best exploit natural vestibular stimulation?

The Zing Performance operation (see Appendix 1) applies a novel exercise-based approach designed to challenge the cerebellum via natural vestibular stimulation and uses an internet-based system for determining the sequence of exercises, for taking feedback from clients, and for illustrating the next exercises. The marginal cost per additional user is therefore essentially zero in operation (except for logistics of client databases etc), though of course there are heavy development costs.

2 The Underlying Science

2.1 Science

In my view this is one of the most critical aspects. It is crucial to demonstrate that the fundamental ideas behind vestibular stimulation are sound, then to understand what Zing Performance does [or can do], then to relate it to the current scientific understanding and frameworks.

2.1.1 What does Zing Performance do?

The general format of Zing Performance is that the user does a set of exercises, modelled via video, one then fills in a progress assessment. If the user does it satisfactorily the next exercise downloaded will be harder etc. Therefore in due course the user gets to a level of difficulty where he/she is struggling to do it. And there are two 10 minute sessions per day. Technically (see Appendix 1), the Zing Performance system involves a series of graded activities on three dimensions – dynamic activity (patterned movement sequences), focus activity (developing the ability both to concentrate and to 'dual task'), and stability activity (coordinative balance).

2.1.1.1 Coordinative Balance

The core activity is coordinative balance. This involves balancing under various conditions, and also involves a range of activities involving unusual head movements while balancing. A particularly interesting one is balancing while putting one's head down towards a shoulder. The rationale behind these activities is 'vestibular stimulation'. The vestibular system includes two components in the 'inner ear', the otoliths (sensitive to gravity and to linear acceleration) and the semi-circular canals (sensitive to horizontality and rotational acceleration) together the vestibular nerve from there to the brain, which synapses on the vestibular nuclei in the brainstem, together with links to the cerebellum, the optic nerves and various body posture nerves. This system allows the brain to monitor head acceleration (linear and rotational) and therefore to adjust gaze and posture so that the body remains upright and the eyes remain fixated on the target despite the movements – the eye fixation is known as the vestibular-ocular reflex and is known to involve cerebellar control for learning and for execution.

Abnormal vestibular input therefore provides a 'challenge' to the cerebellum, because it does not have a suitable learned routine. Proprioceptive feedback from the body will indicate a failure to maintain balance, and this will lead to extensive cerebellar activation in 'error mode'. This activation basically facilitates brain changes, 'shaking' up existing networks, and allowing the connection of brain regions that were previously not connected (under the Hebb rule – cells that fire together wire together).

Success in this type of exercise will specifically improve the body's coordination under abnormal vestibular conditions but may also prime the brain for change and breaking out of old habits.

2.1.1.2 Focus Activities

These are designed to improve attentional performance. The traditional view is of attention as a 'spotlight' that can be adjusted to point at a particular region (vision, audition, internal, top right etc), so improving attention may be seen in terms of intensity, focus and duration. Other important issues, however, relate to breadth – it is valuable to distinguish between focused and ambient attention, with ambient attention relating to ideas such as breadth of attention (ie. keeping track of things that one is not looking at directly), covert attention (although looking at the computer, one is somehow monitoring the doorway) and divided attention (looking at the football while somehow being aware of the positions and calls of all one's team-mates or opponents). It's also worth noting that attention to one dimension means inhibiting processing of other areas, so the concept of inhibition is also important here.

The Zing Performance focus activities fall into two categories: eye tracking activities (designed to improve focal attention – make the spotlight brighter for longer).

2.1.1.3 Dynamic Activities

There is a lack of clarity about exactly what the dynamic activities entail, but this is a central category, which should link to activities that are designed to improve speed of processing, overall coordination of physical and mental processing and ambient attention   The multi-tasking activities (designed to improve non-focal attention). A multi-tasking activity would be to balance while doing something else, thereby preventing conscious attention on the balance task, and forcing the balance to become automatic.

2.2 LINKS TO THE KEY CLAIMS OF THE ZING PERFORMANCE INTERVENTION

The key claims for Zing Performance come under four categories, as shown below:

(i) Vestibular stimulation
(ii) Cerebellar-connection enhancement
(iii) Attentional enhancement
   a. Salience
   b. Cognitive Control
(iv) Executive Function Enhancement
   a. Working Memory
   b. Inhibition
   c. Set shifting

2.2.1 What is the evidence that vestibular stimulation really does hit the spot?

The vestibular stimulation may be seen as a particular form of coordinative exercise (CE). There are many versions of CE, with tai chi being a common one. Basically these are exercises that require difficult and careful movements but no great physical strength or endurance. They contrast with cardiovascular exercises, which are the traditional workout. It's pretty clear that cardiovascular exercises use repetitive pre-learned movements, whereas CE involves the careful learning of new movements so there's a major difference in the recruitment of new brain regions. The evidence comes into three categories: the current views on the effect of exercise on the brain, the specific effects of vestibular stimulation, and the effects of direct cerebellar stimulation. They all strongly support the Zing Performance framework.

a. Effects of exercise on the brain. There is extensive evidence that exercise has beneficial effects for people of all ages, and appears to improve not only physical fitness but also mental fitness, and even stimulates the growth of new brain neurons and connections (Hillman et al., 2008). A recent discovery has been the differential effects of cardiovascular exercise and CE. There is strong evidence that exercise can potentiate the brain for new learning, with coordinative balance exercises leading to neural growth in the hippocampus - a core structure for explicit learning and memory (Niemann et al., 2014) - and also in the cerebellar-cortical loop (Burciu et al., 2013) - a core network for implicit learning and coordination. There is also evidence that even imagining exercising leads to cerebellar activation (Thornton et al., 2001). Recent studies of the effects of exercise on rat brains (J. L. Abel & Rissman, 2013; Kellermann et al., 2012) reveal strong effects on epigenetic changes and in changes in the cerebellar Purkinje cells following a rat vestibular training exercise (Lee, Huang, Huang, Tsai, & Yen, 2015). While not strictly relevant here, there is evidence that BDNF is expressed in the cerebellum following environmental enrichment for rats (Angelucci et al., 2009; Vazquez-Sanroman et al., 2013). Of particular interest, there is evidence (though sparse) that Quadrato exercise (like Tai Chi) led to increased creativity and changes in grey matter and white matter in the cerebellum (Ben-Soussan, Berkovich-Ohana, Piervincenzi, Glicksohn, & Carducci, 2015)
b. Vestibular exercises. These tend to be used specifically for dizziness. Scientific investigations have used specific stimulations as above. A recent review (McDonnell & Hillier, 2015) confirms significant effects in patients and suggests combining with exercise.
c. Direct vestibular stimulation. There are two means of direct vestibular stimulation, caloric (applying heat to the inner ear) and 'galvanic' – dc electrical stimulation of the ear. There is a longstanding but controversial history for both kinds (Fitzpatrick & Day, 2004), with recent reviews confirming their importance. Caloric stimulation highlights a role in body image and sensorimotor processing, and even pain perception (Deroualle, Borel, Deveze, & Lopez, 2015; Ferre, Bottini, Iannetti, & Haggard, 2013; Ferre, Haggard, Bottini, & Iannetti, 2015; Ferre, Walther, & Haggard, 2015; Lopez, Schreyer, Preuss, & Mast, 2012). These studies have led to the realization that the vestibular system is widely represented, and at different timescales throughout the brain, with regions comprising the posterior insula and retro insular regions, the anterior insula and the inferior/middle frontal gyrus, the superior temporal gyrus, the temporoparietal cortex, the pre- and postcentral gyrus, the basal ganglia, the anterior cingulate gyrus, the precuneus, the parahippocampal gyrus and hippocampus, the occipital lobe, the supplementary motor area (SMA) and the cerebellum (Della-Justina et al., 2015; Klingner et al., 2013). A new approach, stochastic vestibular stimulation, is a form of galvanic stimulation with time-varying (white noise) low current (Goel et al., 2015; Mulavara et al., 2011; Mulavara et al., 2015).
d. Direct stimulation of the cerebellum There is also now extensive information about the use of transcranial magnetic stimulation (TMS; single pulse or repetitive (rTMS)) or transcranial direct current stimulation (tDCS; anodal or cathodal). A recent 'consensus' paper (Grimaldi et al., 2014) stresses the need for large scale rigorous studies but concludes "*There is a consensus amongst the panel of experts that both TMS and tDCS can effectively influence cerebellar functions, not only in the motor domain, with effects on visually guided tracking tasks, motor surround inhibition, motor adaptation and learning, but also for the cognitive and affective operations handled by the cerebrocerebellar circuits. Verbal working memory, semantic associations and predictive language processing are amongst these operations. Both TMS and tDCS modulate the connectivity between the cerebellum and the primary motor cortex, tuning cerebellar excitability.*" Recent papers highlight the role also in emotions (Ferre et al., 2013; Ferre, Haggard, et al., 2015) and in body schemas (Lopez et al., 2012). There is also evidence that cerebellar stimulation influences the default network (Halko, Farzan, Eldaief, Schmahmann, & Pascual-Leone, 2014), which I discuss below.
e. Memory Reactivation. The above studies are really interesting, because they highlight the multiple pathways by which activity-based stimulation might be expected to have an effect. In particular, one would predict effects on the (many) systems in which the cerebellum is involved, which means most of the systems that are not available to consciousness, but also the many systems in which the hippocampus is involved, the so-called declarative system, which does involve conscious processing (and spatial processing). There is extensive new (and exciting)

work on the role of the hippocampus, in that it is seen as the gateway to storing and retrieving memories, with the core idea being that the memory plus context is initially stored in the hippocampus, but overnight the memory gets integrated with existing memories in the cortical lobes, and the representation in the hippocampus merely becomes a pointer to this large 'schema' (a bit like Google searching through stuff, archiving it off in offline storage, but saving the pointers…) There's also a great deal of research on how these processes occur naturally during sleep (T. Abel, Havekes, Saletin, & Walker, 2013; Sara, 2010). From the Zing Performance perspective, though, there are two major points. First the idea of memory reconsolidation, which means that memories actually become fragile and modifiable when accessed (Diekelmann, Buechel, Born, & Rasch, 2011; Rasch & Born, 2007; Sara, 2010). Furthermore, stimulating the hippocampus is known to cause neurogenesis (new cells) and these are particularly important for memory restructuring (Sahay et al., 2011; Suarez-Pereira & Carrion, 2015). If the new cells are not used, they die off (apoptosis). It is likely (though less researched) that reactivation also occurs with procedural memories (Schoenauer, Geisler, & Gais, 2014), and the chances are that this is effected through striatal and hippocampal systems (Albouy et al., 2015).

In summary, there is now strong evidence that exercise stimulates the brain generally, including the hippocampus, that cerebellar stimulation leads to a range of changes, and that all of these systems interact with each other. Furthermore, exercise causes neurogenesis (new cells) in the hippocampus and cerebellum, and affects the synaptic strengths in the cerebellum. Referring back to the executive summary, two of the major effects of Zing Performance stimulation will therefore be network co-activation (that is, pretty much all of the brain networks are activated at the same time), neurogenesis (that is, new cells get formed, and synapses also develop), and stochastic challenge (that is, the brain is repeatedly confronted with things it can't do, forcing it to try to change). How about the functional changes!?

2.2.2 Links to the underlying cognitive development / neuroscience (CDN)

The key scientific functional areas of CDN relevant to Zing Performance are intelligence, attention, and executive function. Executive function basically relates to the function of the information processing architecture – working memory, attention, inhibition. Understanding of these constructs – what they are, where they are in the brain, and how they may be measured – has increased dramatically in recent years, though there are significant gaps in knowledge, with different disciplines focusing on local issues and failing to consider the bigger picture.

In terms of the cognitive neuroscience of the brain, the classic approach to identifying brain networks has been through autopsies or via animals, on which direct experiments may be undertaken. In fact these techniques have been developed considerably in recent years, and techniques such as retroviral tracers allows individual nerve pathways to be traced in (just dead) brains. This has led to a range of studies demonstrating that the cerebellum is connected to all the other major structures (Bostan, Dum, & Strick, 2010, 2013; Bostan & Strick, 2010; Coffman, Dum, & Strick, 2011; Hoshi, Tremblay, Feger, Carras, & Strick, 2005) and other studies (Albouy, King, Maquet, & Doyon, 2013; Igloi et al., 2015) have demonstrated the link between the cerebellum, the striatum (basal ganglia) and the hippocampus. Traditionally (Cohen & Squire, 1980; Squire, Knowlton, & Musen, 1993) , the major brain networks are referred to as the declarative circuit (through the hippocampus and frontal lobes of the cortex) and the procedural circuits (through the striatum and cerebellum and motor areas of the cortex), though it is well known that they 'conspire and compete' together, even in cognitive tasks such as language (Ullman, 2004).

Cognitive neuroscience has been transformed by new methods of brain imaging were developed in the late 1980s that allow brain structure and function to be assessed. These include Positron Emission Tomography (PET) and functional and structural Magnetic Resonance Imaging (fMRI and sMRI). Structural MRI is limited in that it delineates brain slices but does not show the underlying networks. Following these developments, new approaches include Diffusion Tensor Imaging (DTI) which is a form of sMRI that tracks the direction of movement of water in each brain voxel, thereby allowing the inference of where the brain tracts (white matter) go. Further developments of DTI have been developed to address the tricky problem of how to cope when several tracts go through the same voxel. A major recent development has been the pooling of brain scans, so that composite findings from any studies may be aggregated, and meta-analyses undertaken, thereby providing strong data on which areas are involved in what activities. The traditional approach to inferring brain function has been the subtractivity method - get the fMRI of the brain at rest (or just looking at a fixation point), then get the activity when say the stimulus is presented, then subtract the two activities and infer that the difference reflects the processing of the stimulus. One slowly builds up one extra task at a time to try to find the additional areas recruited.

One recent and highly promising development has been intrinsic connectivity (IC) analysis. This exploits the fact that if there are brain networks (unfortunately this can't really be found out easily from fMRI or sMRI) then the activities in these networks should somehow be in phase – like a Mexican Wave – a sort of large scale Hebb rule). Consequently investigation of slow oscillations in brain regions allows one to infer the underlying networks. The earliest such example was an analysis of the actual rest state (which as we have seen is fundamental to the subtractivity method for fMRI), because many researchers had noticed that the brain was in no way inactive in the rest state, with all sorts of activities going on. The IC analysis of the Resting state allowed the identification of the Default Network (what the brain is doing when not doing anything else…), and other analyses have led to the identification of various other networks which are in use in various tasks.

Seven key networks have been identified (Bernard et al., 2012; Buckner, Krienen, Castellanos, Diaz, & Yeo, 2011), namely `The Default Network (or Default Mode Network) (Buckner, Andrews-Hanna, & Schacter, 2008) is engaged when a person is not actively doing anything, and can be involved in thinking about others, thinking about themselves, remembering the past, and planning for the future. The somatomotor network relates to the body and to motor coordination. Three others of the 7 networks are related to attention. The dorsal attentional network is thought to mediate the top-down guided voluntary allocation of attention to locations or features (Vossel, Geng, & Fink, 2014). The ventral attentional network is alternatively termed the Cingulo-Opercular network, and is often labelled the salience network. The fronto-parietal network seems to initiate and adjust control; the cingulo-opercular component provides stable 'set-maintenance' over entire task epochs" (Dosenbach, Fair, Cohen, Schlaggar, & Petersen, 2008). Of crucial significance here, although the original studies excluded the cerebellum, more recent work has demonstrated that the cerebellum is a core component of all 7 networks – and indeed another 10 common networks (Buckner et al., 2011).

2.2.3 Executive Functions

Early information processing models distinguished between the 'central executive', which somehow did all the active processing, and was equated with the conscious controller, and various other aspects of the brain architecture such as long term memory. The idea of an executive function (a process undertaken by the central executive, but more frequently a capability shown by the executive executive) has come into vogue in recent years. Most current cognitive neuroscience discussions focus on the executive functions or attention (which for some reason is not included).

"*Core Executive Functions are inhibition [response inhibition (self-control—resisting temptations and resisting acting impulsively) and interference control (selective attention and cognitive inhibition)], working memory, and cognitive flexibility (including creatively thinking "outside the box," seeing anything from different perspectives, and quickly and flexibly adapting to changed circumstances)*" (Diamond, 2013).

A more specific classification that relates well to current cognitive neuroscience formulations was proposed by (Miyake & Friedman, 2012) "*Our research has focused primarily on three Executive Functions: updating (constant monitoring and rapid addition/deletion of working memory contents),* *shifting (switching flexibly between tasks or mental sets), and inhibition (deliberate overriding of dominant or prepotent responses).”*

2.3 THE SCIENCE OF NEURAL PLASTICITY

Significant progress has been made recently in the understanding of the mechanisms of ‘neural plasticity’ (NP) – the way that the brain’s cells and networks develop and adapt with experience. The core dilemma for NP is how to achieve adaptive change without interfering with the existing knowledge and functions. In a simplistic approach, new knowledge, functions and networks would simply overwrite, or displace access to, older knowledge, functions and networks. Plasticity is a good description because it highlights the limitations to change.

This balancing act – between change and stability – is endemic for all organizations, from the brain to the individual to the team to the organization to society. The historically unprecedented ‘adaptability pressures’ brought about by 21st century challenges – from social technologies to artificial intelligence to over-population to climate change – highlight the need for individuals to be able to adapt continually to changing circumstances. Unfortunately, although the brain retains some plasticity into old age, in general, plasticity declines very markedly from infancy to childhood to adulthood to maturity to old age. It is therefore of crucial importance to better understand, and hence to develop methods to facilitate, plasticity at the different stages in the lifespan.

The advent of new brain imaging techniques has transformed our ability to investigate the processes of NP, but nonetheless we are in a state of rapid change in understanding, with very clear limitations on current scientific knowledge. Plasticity occurs on many levels – from the creation of new brain cells (neurogenesis), to development of new connections (synapses) between cells, to changes in the ‘strength’ of synaptic connections, to the creation of neural circuits connecting different brain regions, to the refinement of these circuits to work faster and more efficiently. Many of these challenges faced by the brain have direct analogies with any organism needing to adapt, and the solutions adopted show ‘convergent evolution’ with such organisms, and this equivalence at the ‘challenge’ level allows us to provide a range of metaphors that allow us to better understand NP. First I will state three fundamental ‘rules’ of MNP.

2.3.1 Four Principles of Neural Plasticity

(i) The ‘Connective growth’ rule - find a friend. Cells sprout dendrites, then the dendrites grow in random directions through the brain until they are able to synapse onto the dendrites of another cell (with each cell type predisposed to prefer a specific type of target cell).

(ii) The ‘Hebb Rule’ – cells that fire together wire together. This is the fundamental excitatory rule and applies both at cell level and network level.

(iii) The ‘utility rule’ – use it or lose it. If the firing in a given synapse is not correlated with other firing patterns, reduce the connection strength. This applies at the between-cell level.

(iv) The ‘homeostatic rule’ – if it ain’t broke don’t fix it – this is the fundamental stability rule, and applies at the network level.

In general these changes are not initially permanent, typically they need to be consolidated, often overnight, and actually stored somewhere else– to take a computer analogy, moving from RAM to permanent all storage.

The brain has several ways of stimulating neural plasticity. A lot of this is down to genes, which when expressed can lead to greater plasticity. For example, in adolescence a whole range of changes take place genetically preprogrammed. Gene expression typically involves neurotrophic factors, that is hormones that stimulate the growth.

2.3.2 Metaphors for Neural Plasticity

(i) Tropical creeper. At the cellular level, it is crucial to recognize that the cells in the brain are living and growing entities, perhaps like a Virginia creeper, sending out shoots and trying to connect to everything in their reach. They rapidly 'synapse' onto other cells, with the strength of the connection increasing following the Hebb Rule (and decreasing if there is no joint firing)

(ii) Canal system. At the neural circuit level, a useful metaphor is in terms of a canal system. The flow of information through the cells and synapses of the circuit may be considered as water flowing through the canals. The faster the volume and flow of water the better the brain's function, but if one thinks of the flow digging deeper channels over time, leading to some changes in the main channel and perhaps some ox-bow lakes that are no longer connected to the main channels, this gives a feel for how major circuits build up.

(iii) Computing system. We must of course also maintain the computer system metaphor, with the idea of information travelling around the circuit, being transformed from one format to another. This also provides a valuable metaphor for how the change/stabilise dilemma may be resolved, in that for a computer one has the Random Access Memory is used for current (short term) processing, but in order foe

2.4 PROCESSES OF NP

Consider five convincing demonstrations of NP

2.4.1 Blakemore's kittens

The authors reared kittens in an environment with only horizontal lines (Blakemore & Cooper, 1970). The kittens did not develop the ability to 'see' vertical lines, but did do so if they were then exposed to vertical lines within the 'sensitive period' of 3-6 weeks from birth. Otherwise they never developed the ability.

2.4.2 Merzenich's monkeys

The authors trained adult monkeys to discriminate tones around the 2500 Hz frequency (Recanzone, Schreiner, & Merzenich, 1993) – see https://computervisionblog.wordpress.com/2013/06/01/cats-and-vision-is-vision-acquired-or-innate/. Following training, the 'receptive field' in the auditory cortex were very much skewed to the 2000-3000 Hz range, showing that the environmental importance of these sounds led to 'colonization' of neighboring regions of the auditory cortex which had previously been tuned to a different frequency range.

2.4.3 Imamizu's adults

The authors presented adults with a 'reverse mouse' (which had been modified to move the cursor left with a rightward movement and vice versa) and monitored functional activity in the brain. Two phases of activity were identified. In the initial phase the entire cerebellum, was highly active. The authors interpreted this in terms of error identification. The learned mouse control movements failed, leading to error signals throughout the cerebellum. In the second phase, after the new skill had been learned, there was almost no cerebellar activation, but sophisticated analyses revealed a single small region of activation corresponding to cerebellar circuit smoothly completing the task. This study reveals the role of the cerebellum both in manual control and in error detection.

2.4.4 Sandin's Bike

In this video •https://www.youtube.com/watch?v=MFzDaBzBlL0 Smarter Every Day vlogger Dustin Sandin demonstrates the near-impossibility of re-learning to ride a bicycle that has had its handlebars re-engineered similar to Imamizu's study above, so that pulling the left hand backwards moves the front wheel to the right. It took him 8 months to learn to ride this bike by which point he had lost the ability to ride an ordinary bike (but rediscovered the skill in about 15 minutes). His young son, despite 4 years of bike-riding experience, learned the reverse bike much more easily.

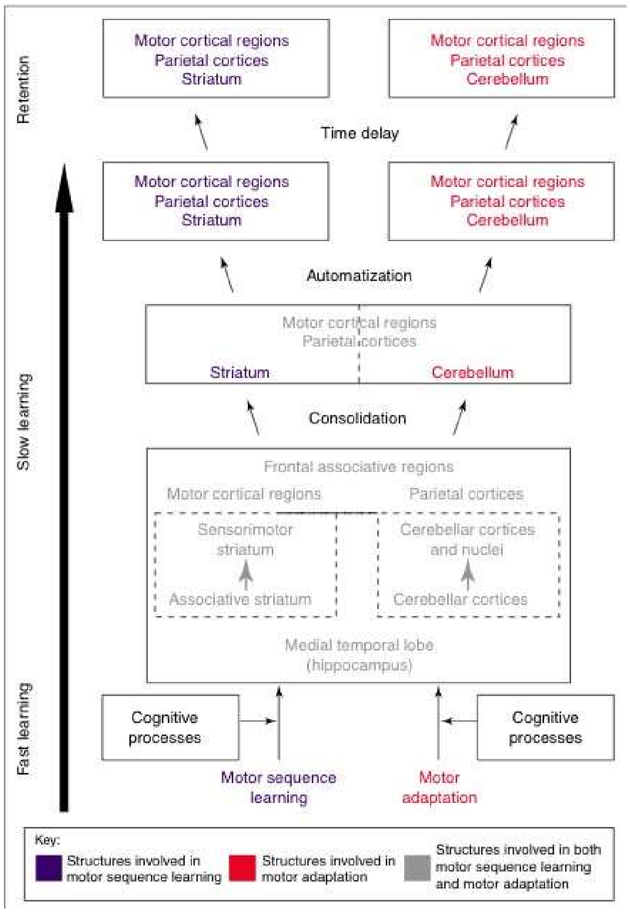
2.4.5 Lametti's Cerebellar Stimulation

Tbe authors (Lametti, Smith, Freidin, & Watkins, 2018) modified, in real time, the first formant of speech made such that *head, bed,* and *dead* sounded (to the speaker) more like *had, bad,* and *dad* respectively, and monitored the speed and quality of the subsequent speech adaptation. A key innovation was the use of transcranial direct current stimulation (tDCS) to different brain regions. They contrasted cerebellar tDCS, motor cortex tDCS and sham tDCS. They concluded (p. 540) *"Motor cortex tDCS drove production changes that offset errors in the first formant, but unlike cerebellar tDCS, adaptive changes in the second formant also occurred. The results suggest that motor cortex and cerebellar tDCS have both shared and dissociable effects on motor adaptation. The study provides initial causal evidence in speech production that the motor cortex and the cerebellum support different aspects of sensorimotor learning. We propose that motor cortex tDCS drives sensorimotor learning toward previously learned patterns of movement, whereas cerebellar tDCS focuses sensorimotor learning on error correction."* This is a major finding, directly relevant to Zing Performance, in that the Zing Performance exercises may be seen as a natural form of cerebellar stimulation.

2.5 TIMESCALES OF NP

The most complete current model of the involvement of different brain regions in the various stages and types of skill is provided by Doyon and Ungerleider (Doyon & Benali, 2005; Doyon, Penhune, & Ungerleider, 2003; Doyon & Ungerleider, 2002). The key point of the Doyon / Ungerleider model is that there are two distinct motor learning circuits, a cortico-striatal system and a cortico-cerebellar system. One of the distinctive aspects of the model is that they distinguish the contributions made by these systems. They propose that "*experience-dependent changes in the brain depend not only on the stage of learning, but also on whether subjects are required to learn a new sequence of movements (motor sequence learning) or learn to adapt to environmental perturbations (motor adaptation). This model proposes that the cortico-striatal and cortico-cerebellar systems contribute differentially to motor sequence learning and motor adaptation, respectively, and that this is most apparent during the slow learning phase (i.e. automatization) when subjects achieve asymptotic performance, as well as during reactivation of the new skilled behavior in the retention phase*" . The key point for us here is that all three brain regions – motor cortex, basal ganglia and cerebellum (and, we presume, frontal cortex for explicit skill monitoring in the early stages) are involved in the initial stage of motor skill acquisition, whereas the roles of the cortico-striatal and cortico-cerebellar systems diverge as we approach the automatization stage (figure 3).

Figure 3: Procedural Learning: Striatal and Cerebellar contributions



Procedural learning corresponds to the powerful and evolutionarily ancient 'brain-based' built-in learning processes that take place following the various learning rules outlined above. Humans have a further 'declarative learning' capability under conscious control, typically using language and thought processes (labelled as 'cognitive processes in the above figure). The hub for declarative learning is the hippocampus, a structure in the medial temporal lobe and part of the limbic system, together with many linked regions of cerebral cortex. A complementary time-scale analysis may be made for the processes of declarative learning and consolidation, with fast learning occurring locally in the hippocampus, with the products then integrated with existing knowledge and consolidated in the slow learning phase. The two-stage model of memory consolidation (Diekelmann, 2014) is that the hippocampus acts as a rapidly-changing, transient, memory store, and during slow wave sleep it interacts with longer-term, stable stores in the cortex to transfer the information and also to allow 'system consolidation' – integrating the new memories with existing memories. By contrast, in REM (Rapid Eye Movement) sleep there is synaptic consolidation (strengthening) of the newly integrated systems in the long-term stores. Interestingly, it appears that the declarative memory circuits become susceptible to change through a process of 'memory reactivation', and this process can be exploited to enhance consolidation and recall (Feld & Diekelmann, 2015). It is likely that similar processes occur for procedural learning though less dependent on sleep (Galea, Vazquez, Pasricha, de Xivry, & Celnik, 2011; King, Hoedlmoser, Hirschauer, Dolfen, & Albouy, 2017).

2.6 WHAT ARE THE IDEAL CONDITIONS FOR INDUCING NP?

In analogy with the rainforest, ideal conditions for NP include the following:

Appropriate nutrients. As with plants, there are many important brain nutrients, the substances underpinning the creation of neurotransmitters and cell maintenance and plasticity processes. Recent reviews suggest omega-3 fatty acids, dietary polyphenols such as curcumin and flavonoids such as berries and green tea (Gomez-Pinilla, 2008; Gomez-Pinilla & Gomez, 2011). Interestingly, it appears that such dietary enhancements work synergistically with te effects of exercise.

Fertile growing conditions – in brains, the neurotrophins helps to support the survival of existing neurons, and encourage the growth and differentiation of new neurons and synapses through axonal and dendritic sprouting. The two major neurotrophins are BDNF (brain-derived neurotrophic factor), which is active in the hippocampus, cortex, cerebellum and basal forebrain; and NGF (Nerve growth factor) which is centrally involved in survival and maintenance of sympathetic and sensory neurones and is also secreted in the cerebral cortex and hypothalamus.

Energy sources. For plants the key energy source for photosynthesis are carbon dioxide and sunlight. In the brain, oxygen plus nutrients from the blood are used to fuel cell metabolism via the mitochondria.

Excitation. Unlike plants, cells need excitation – neural firing. As noted, the Hebb rule is the key driver in growth of synaptic strength. There are background rates of activation, and therefore it is abnormal activation rate that drives these changes.

Trigger stimulus. For plants there are of course growing seasons, with the trigger for new growth being soil temperature or humidity, after which new phases may be triggered by environmental events or gene expression. For humans there are global triggers such as puberty, but there are also situational triggers, typically some sort of 'challenge', such as described above where the brain is faced by a problem it cannot solve using its existing routines. In fact, response to a challenge could go two ways. If the challenge is seen as a threat, it is likely that the hypothalamic–pituitary–adrenal (HPA) axis will be stimulated, leading to 'freeze' or avoidance actions, together with blood diversion to the muscles. By contrast, it may be that a challenge is seen as an opportunity, thereby resulting in secretion of BDNF, possible neurogenesis and blood flow to the region in question.

APPENDIX 1: THE ZING PERFORMANCE INTERVENTION SYSTEM

Zing Background and development

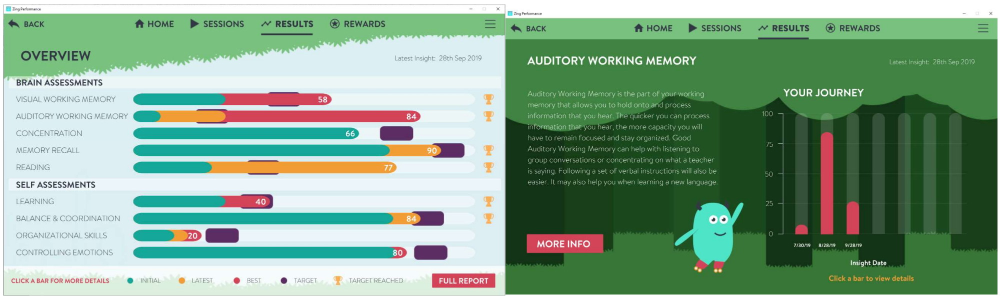
Since 2010 Zing Performance has been inspired by recent discoveries in neuroscience to develop a personalized online programme made up of simple physical activities to help improve a person's overall performance. It has focused on piecing together this latest research to develop programmes that can be personalized to the developmental needs of each individual. The crucial element of such programmes is that they are engaging so that participants adhere to the course to achieve the potential benefits. Great focus has been placed on using proven and reliable methods of assessing existing brain skills so that a baseline is established to show progress during the course and also to help with the prescription of specific activities required to suit the current level of the user's ability.

As new research gets released this is scrutinized to see if anything can be gleaned that will enhance the existing product in any way. Alongside this, the technical team are committed to carefully watching future trends in technology to ensure that the whole system is future-proofed. The technology used is capable of delivery on all common platforms including ios, android, PC and Mac together with a wide variety of other games type platforms.

This programme was originally developed to tune up the coordination abilities of top sporting performers, using a series of graded exercises designed specifically to improve three performance dimensions: sensorimotor coordination, eye movement control, and dual tasking. However, extensive feedback had suggested that the programme was also valuable for many average performers. Consequently the system was embedded in an internet-based 'game' format designed to challenge and stimulate the user to keep improving their performance. Zing Performance offer a number of courses specifically tailored to each individual user, with applications in sporting areas and in education. The Zing Performance system involves a series of graded activities on three dimensions – dynamic activity (patterned movement sequences), focus activity (developing the ability both to concentrate and to 'dual task'), and stability activity (coordinative balance). Illustrations of the current interface are shown in Figure 1-2A and B.

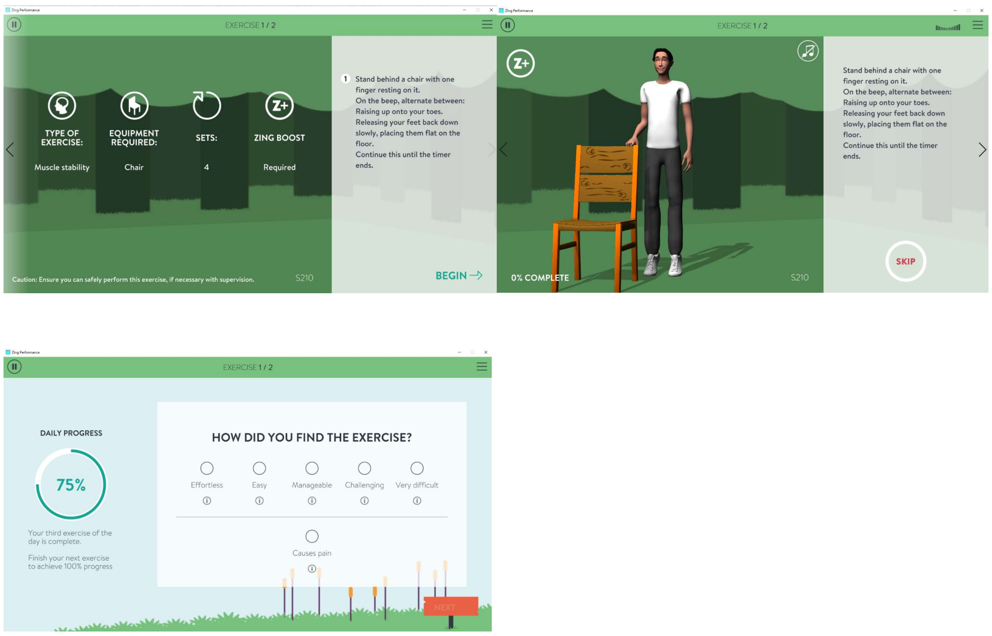
The key to the assessment and reporting capabilities of Zing Performance are the 'Insight' suite of assessment programs. Users complete the 30 minute Insight test battery initially, and on the basis of their performance a series of targets for their future development are created using proprietary expert system software. The Insight tests are repeated every 30 days. Progress is explicitly displayed on the Report, providing motivating evidence of improvements toward the target performance on the dimensions relevant to the user's specific goals.

2.7 FIGURE 1-2A: THE ZING PERFORMANCE 'INSIGHT' ASSESSMENT AND REPORTING SYSTEM



The core to Zing Performance is the adaptive coordinative exercise activities designed to stimulate the cerebellum and related brain circuits through vestibular activity. A typical Zing Performance Session is shown in Figure 1-3B. The session is downloaded over the internet (to phone, tablet or computer), the text on the left gives the required instructions, which are illustrated using the video clip on the right of the avatar undertaking the exercise in question.

2.8 Figure 1-3B: The Zing Performance Activities



REFERENCES

Abel, Jean LeBeau, & Rissman, Emilie F. (2013). Running-induced epigenetic and gene expression changes in the adolescent brain. *International Journal of Developmental Neuroscience, 31*(6), 382-390.

Abel, Ted, Havekes, Robbert, Saletin, Jared M., & Walker, Matthew P. (2013). Sleep, Plasticity and Memory from Molecules to Whole-Brain Networks. *Current Biology, 23*(17), R774-R788.

Albouy, Genevieve, Fogel, Stuart, King, Bradley R., Laventure, Samuel, Benali, Habib, Karni, Avi, . . . Doyon, Julien. (2015). Maintaining vs. enhancing motor sequence memories: Respective roles of striatal and hippocampal systems. *Neuroimage, 108*, 423-434.

Albouy, Genevieve, King, Bradley R., Maquet, Pierre, & Doyon, Julien. (2013). Hippocampus and Striatum: Dynamics and Interaction During Acquisition and Sleep-Related Motor Sequence Memory Consolidation. *Hippocampus, 23*(11), 985-1004.

Angelucci, Francesco, De Bartolo, Paola, Gelfo, Francesca, Foti, Francesca, Cutuli, Debora, Bossu, Paola, . . . Petrosini, Laura. (2009). Increased Concentrations of Nerve Growth Factor and Brain-Derived Neurotrophic Factor in the Rat Cerebellum After Exposure to Environmental Enrichment. *Cerebellum, 8*(4), 499-506.

Ben-Soussan, Tal D., Berkovich-Ohana, Aviva, Piervincenzi, Claudia, Glicksohn, Joseph, & Carducci, Filippo. (2015). Embodied cognitive flexibility and neuroplasticity following Quadrato Motor Training. *Frontiers in psychology, 6*.

Bernard, Jessica A., Seidler, Rachael D., Hassevoort, Kelsey M., Benson, Bryan L., Welsh, Robert C., Wiggins, Jillian Lee, . . . Peltier, Scott J. (2012). Resting state cortico-cerebellar functional connectivity networks: a comparison of anatomical and self-organizing map approaches. *Frontiers in Neuroanatomy, 6*.

Blakemore, C., & Cooper, G. F. (1970). Development of Brain Depends on Visual Environment. *Nature, 228*(5270), 477-+.

Bostan, Andreea C., Dum, Richard P., & Strick, Peter L. (2010). The basal ganglia communicate with the cerebellum. *Proceedings of the National Academy of Sciences of the United States of America, 107*(18), 8452-8456.

Bostan, Andreea C., Dum, Richard P., & Strick, Peter L. (2013). Cerebellar networks with the cerebral cortex and basal ganglia. *Trends in Cognitive Sciences, 17*(5), 241-254.

Bostan, Andreea C., & Strick, Peter L. (2010). The Cerebellum and Basal Ganglia are Interconnected. *Neuropsychology Review, 20*(3), 261-270.

Buckner, Randy L., Andrews-Hanna, Jessica R., & Schacter, Daniel L. (2008). The brain's default network - Anatomy, function, and relevance to disease. In A. Kingstone & M. B. Miller (Eds.), *Year in Cognitive Neuroscience 2008* (Vol. 1124, pp. 1-38).

Buckner, Randy L., Krienen, Fenna M., Castellanos, Angela, Diaz, Julio C., & Yeo, B. T. Thomas. (2011). The organization of the human cerebellum estimated by intrinsic functional connectivity. *Journal of Neurophysiology, 106*(5), 2322-2345.

Burciu, Roxana Gabriela, Fritsche, Nicole, Granert, Oliver, Schmitz, Lutz, Spoenemann, Nina, Konczak, Juergen, . . . Timmann, Dagmar. (2013). Brain Changes Associated with Postural Training in Patients with Cerebellar Degeneration: A Voxel-Based Morphometry Study. *Journal of Neuroscience, 33*(10), 4594-4604. doi: 10.1523/jneurosci.3381-12.2013

Coffman, Keith A., Dum, Richard P., & Strick, Peter L. (2011). Cerebellar vermis is a target of projections from the motor areas in the cerebral cortex. *Proceedings of the National Academy of Sciences of the United States of America, 108*(38), 16068-16073.

Cohen, N. J., & Squire, L. R. (1980). Preserved learning and retention of pattern analyzing skill in amnesia: Dissociation of knowing how and knowing that. *Science, 210*, 207-209.

Della-Justina, H. M., Gamba, H. R., Lukasova, K., Nucci-da-Silva, M. P., Winkler, A. M., & Amaro, E. (2015). Interaction of brain areas of visual and vestibular simultaneous activity with fMRI. *Experimental Brain Research, 233*(1), 237-252.

Deroualle, Diane, Borel, Liliane, Deveze, Arnaud, & Lopez, Christophe. (2015). Changing perspective: The role of vestibular signals. *Neuropsychologia, 79*(B), 175-185.

Diamond, Adele. (2013). Executive Functions. *Annual Review of Psychology, Vol 64, 64*, 135-168.

Diekelmann, Susanne. (2014). Sleep for cognitive enhancement. *Frontiers in systems neuroscience, 8*, 46-46.

Diekelmann, Susanne, Buechel, Christian, Born, Jan, & Rasch, Bjoern. (2011). Labile or stable: opposing consequences for memory when reactivated during waking and sleep. *Nature Neuroscience, 14*(3), 381-386.

Dosenbach, Nico U. F., Fair, Damien A., Cohen, Alexander L., Schlaggar, Bradley L., & Petersen, Steven E. (2008). A dual-networks architecture of top-down control. *Trends in Cognitive Sciences, 12*(3), 99-105.

Doyon, J., & Benali, H. (2005). Reorganization and plasticity in the adult brain during learning of motor skills. *Current Opinion in Neurobiology, 15*, 1-7.

Doyon, J., Penhune, V., & Ungerleider, L. G. (2003). Distinct contribution of the cortico-striatal and cortico- cerebellar systems to motor skill learning. *Neuropsychologia, 41*(3), 252-262.

Doyon, J., & Ungerleider, L. G. (2002). Functional anatomy of motor skill learning. In L. R. Squire & D. L. Schacter (Eds.), *Neuropsychology of memory*. New York: Guilford Press.

Feld, Gordon B., & Diekelmann, Susanne. (2015). Sleep smart-optimizing sleep for declarative learning and memory. *Frontiers in psychology, 6*.

Ferre, Elisa Raffaella, Bottini, Gabriella, Iannetti, Gian Domenico, & Haggard, Patrick. (2013). The balance of feelings: Vestibular modulation of bodily sensations. *Cortex, 49*(3), 748-758.

Ferre, Elisa Raffaella, Haggard, Patrick, Bottini, Gabriella, & Iannetti, Gian Domenico. (2015). Caloric vestibular stimulation modulates nociceptive evoked potentials. *Experimental Brain Research, 233*(12), 3393-3401.

Ferre, Elisa Raffaella, Walther, Leif Erik, & Haggard, Patrick. (2015). Multisensory Interactions between Vestibular, Visual and Somatosensory Signals. *Plos One, 10*(4).

Fitzpatrick, R. C., & Day, B. L. (2004). Probing the human vestibular system with galvanic stimulation. *Journal of Applied Physiology, 96*(6), 2301-2316.

Galea, J. M., Vazquez, A., Pasricha, N., de Xivry, J. J. O., & Celnik, P. (2011). Dissociating the Roles of the Cerebellum and Motor Cortex during Adaptive Learning: The Motor Cortex Retains What the Cerebellum Learns. *Cerebral Cortex, 21*(8), 1761-1770.

Gallant, Z., & Nicolson, R. I. (2017). "Cerebellar Challenge" for Older Adults: Evaluation of a Home-Based Internet Intervention. *Frontiers in aging neuroscience, 9*.

Goel, Rahul, Kofman, Igor, Jeevarajan, Jerome, De Dios, Yiri, Cohen, Helen S., Bloomberg, Jacob J., & Mulavara, Ajitkumar P. (2015). Using Low Levels of Stochastic Vestibular Stimulation to Improve Balance Function. *Plos One, 10*(8).

Gomez-Pinilla, F. (2008). Brain foods: the effects of nutrients on brain function. *Nature Reviews Neuroscience, 9*(7), 568-578.

Gomez-Pinilla, F., & Gomez, A. G. (2011). The Influence of Dietary Factors in Central Nervous System Plasticity and Injury Recovery. *Pm&R, 3*(6), S111-S116.

Grimaldi, G., Argyropoulos, G. P., Boehringer, A., Celnik, P., Edwards, M. J., Ferrucci, R., . . . Ziemann, U. (2014). Non-invasive Cerebellar Stimulation-a Consensus Paper. *Cerebellum, 13*(1), 121-138.

Halko, Mark A., Farzan, Faranak, Eldaief, Mark C., Schmahmann, Jeremy D., & Pascual-Leone, Alvaro. (2014). Intermittent Theta-Burst Stimulation of the Lateral Cerebellum Increases Functional Connectivity of the Default Network. *Journal of Neuroscience, 34*(36), 12049-12056.

Hillman, Charles H., Erickson, Kirk I., & Kramer, Arthur F. (2008). Be smart, exercise your heart: exercise effects on brain and cognition. *Nature Reviews Neuroscience, 9*(1), 58-65. doi: 10.1038/nrn2298

Hoshi, E., Tremblay, L., Feger, J., Carras, P. L., & Strick, P. L. (2005). The cerebellum communicates with the basal ganglia. *Nature Neuroscience, 8*(11), 1491-1493.

Igloi, Kinga, Doeller, Christian F., Paradis, Anne-Lise, Benchenane, Karim, Berthoz, Alain, Burgess, Neil, & Rondi-Reig, Laure. (2015). Interaction Between Hippocampus and Cerebellum Crus I in Sequence-Based but not Place-Based Navigation. *Cerebral cortex (New York, N.Y. : 1991), 25*(11), 4146-4154.

Kellermann, Thilo, Regenbogen, Christina, De Vos, Maarten, Moessnang, Carolin, Finkelmeyer, Andreas, & Habel, Ute. (2012). Effective Connectivity of the Human

Cerebellum during Visual Attention. *Journal of Neuroscience, 32*(33), 11453-11460.

King, B. R., Hoedlmoser, K., Hirschauer, F., Dolfen, N., & Albouy, G. (2017). Sleeping on the motor engram: The multifaceted nature of sleep-related motor memory consolidation. *Neuroscience and Biobehavioral Reviews, 80*, 1-22.

Klingner, C. M., Volk, G. F., Flatz, C., Brodoehl, S., Dieterich, M., Witte, O. W., & Guntinas-Lichius, O. (2013). Components of vestibular cortical function. *Behavioural Brain Research, 236*, 194-199.

Lametti, D. R., Smith, H. J., Freidin, P. F., & Watkins, K. E. (2018). Cortico-cerebellar Networks Drive Sensorimotor Learning in Speech. *Journal of Cognitive Neuroscience, 30*(4), 540-551.

Lee, Ray X., Huang, Jian-Jia, Huang, Chiming, Tsai, Meng-Li, & Yen, Chen-Tung. (2015). Plasticity of cerebellar Purkinje cells in behavioral training of body balance control. *Frontiers in Systems Neuroscience, 9*.

Li, K. Z. H., Bherer, L., Mirelman, A., Maidan, I., & Hausdorff, J. M. (2018). Cognitive Involvement in Balance, Gait and Dual-Tasking in Aging: A Focused Review From a Neuroscience of Aging Perspective. *Frontiers in Neurology, 9*.

Lopez, Christophe, Schreyer, Helene-Marianne, Preuss, Nora, & Mast, Fred W. (2012). Vestibular stimulation modifies the body schema. *Neuropsychologia, 50*(8), 1830-1837.

McDonnell, M. N, & Hillier, S. L. (2015). Vestibular rehabilitation for unilateral peripheral vestibular dysfunction (Review). *Cochrane Database of Systematic Reviews*(1). doi: 10.1002/14651858.CD005397.pub4.

Miyake, A., & Friedman, N. P. (2012). The Nature and Organization of Individual Differences in Executive Functions: Four General Conclusions. *Current Directions in Psychological Science, 21*(1), 8-14.

Mulavara, Ajitkumar P., Fiedler, Matthew J., Kofman, Igor S., Wood, Scott J., Serrador, Jorge M., Peters, Brian, . . . Bloomberg, Jacob J. (2011). Improving balance function using vestibular stochastic resonance: optimizing stimulus characteristics. *Experimental Brain Research, 210*(2), 303-312.

Mulavara, Ajitkumar P., Kofman, Igor S., De Dios, Yiri E., Miller, Chris, Peters, Brian T., Goel, Rahul, . . . Bloomberg, Jacob J. (2015). Using low levels of stochastic vestibular stimulation to improve locomotor stability. *Frontiers in Systems Neuroscience, 9*.

Niemann, Claudia, Godde, Ben, & Voelcker-Rehage, Claudia. (2014). Not only cardiovascular, but also coordinative exercise increases hippocampal volume in older adults. *Frontiers in aging neuroscience, 6*, 170-170. doi: 10.3389/fnagi.2014.00170

Rasch, Bjoern, & Born, Jan. (2007). Maintaining memories by reactivation. *Current Opinion in Neurobiology, 17*(6), 698-703.

Recanzone, G. H., Schreiner, C. E., & Merzenich, M. M. (1993). Plasticity in the frequency representation of primary auditory-cortex following discrimination-training in adult owl monkeys. *Journal of Neuroscience, 13*(1), 87-103.

Reynolds, D., Nicolson, R. I., & Hambly, H. (2003). Evaluation of an exercise-based treatment for children with reading difficulties. *Dyslexia, 9*(1), 48-71.

Sahay, A., Scobie, K. N., Hill, A. S., O'Carroll, C. M., Kheirbek, M. A., Burghardt, N. S., . . . Hen, R. (2011). Increasing adult hippocampal neurogenesis is sufficient to improve pattern separation. *Nature, 472*(7344), 466-U539.

Sara, Susan J. (2010). Reactivation, retrieval, replay and reconsolidation in and out of sleep: connecting the dots. *Frontiers in Behavioral Neuroscience, 4*.

Schoenauer, Monika, Geisler, Teresa, & Gais, Steffen. (2014). Strengthening Procedural Memories by Reactivation in Sleep. *Journal of Cognitive Neuroscience, 26*(1), 143-153.

Squire, L. R. , Knowlton, B., & Musen, G. (1993). The structure and organisation of memory. *Annual Review of Psychology, 44*, 453-495.

Suarez-Pereira, Irene, & Carrion, Angel M. (2015). Updating stored memory requires adult hippocampal neurogenesis. *Scientific Reports, 5*.

Thornton, J. M., Guz, A., Murphy, K., Griffith, A. R., Pedersen, D. L., Kardos, A., . . . Paterson, D. J. (2001). Identification of higher brain centres that may encode the cardiorespiratory response to exercise in humans. *Journal of Physiology-London, 533*(3), 823-836.

Ullman, M. T. (2004). Contributions of memory circuits to language: the declarative/procedural model. *Cognition, 92*(1-2), 231-270.

Vazquez-Sanroman, D., Sanchis-Segura, C., Toledo, R., Hernandez, M. E., Manzo, J., & Miquel, M. (2013). The effects of enriched environment on BDNF expression in the mouse cerebellum depending on the length of exposure. *Behavioural Brain Research, 243*, 118-128.

Vossel, Simone, Geng, Joy J., & Fink, Gereon R. (2014). Dorsal and Ventral Attention Systems: Distinct Neural Circuits but Collaborative Roles. *Neuroscientist, 20*(2), 150-159.