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Cognitive Rehabilitation in Developmental Disabilities

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INTRODUCTION

Cognitive-Motor Development and Dysfunction

Little difference exists between the development of cognitive and motor function in childhood and the relearning of cognitive and motor function post-trauma in adulthood. "Rehabilitation recapitulates phylogeny." In all cases, function must either be learned or re-learned. That learning developmentally is associated with the formation and integration of motor and cognitive milestones.

Motor and Cognitive Effects of Inhibition and Disinhibition as a Basis for Cognitive Rehabilitation

It has been known that individuals who are markedly late in achieving developmental milestones are at high risk for subsequent cognitive impairment [1,2]. The mechanisms underlying infant and adult motor and cognitive associations remain poorly characterized. One possibility is that the

neural systems that subserve motor development in infancy also contribute to the development and operation of specific cognitive processes later in life. Factors related to efficiencies in such systems may be reflected in both rapid motor developments early in life and subsequently in improved cognitive functions [3,4]. However, a number of questions remain concerning the specificity of associations between infant development and later cognitive functions, which, if they could be answered, could shed light on the reasons behind the associations. For example, is the effect confined to infant motor development, or does it also apply to other developmental domains, such as language? Is the effect confined to specific domains of cognition (e.g., executive function), or does it also apply to general intellectual function? Murray and colleagues [4] examined these questions in a large British general population birth cohort in which measurements were available for development in language and motor domains in infancy, general intellectual function in childhood and adolescence, and specific neuropsychological function (e.g., verbal fluency, a test of executive/frontal lobe function) in adulthood. These authors noted that [4] noted that faster attainment of motor developmental milestones is related to better adult cognitive performance in some domains, such as executive function.

The developing infant is concerned with navigating to items of interest and exploring the environment, ultimately to develop a sense of self, independent of the environment to which he or she is circumnavigating. The central idea concerns the influence on a proceeding (or currently planned) muscular act [5]. That influence stems from motivation-triggered anticipation of the act's outcome, and it is conjectured to prevail only if "consciousness" is present [6].

Because motivation relates to the self, while an act's consequences can include environmental components, consciousness is seen as lying at the operational interface between body movement and the body's surroundings. Anticipation is mediated by specific anatomical features, the independent functioning of which, underlies thought simulation of the body's (sometimes passive) transactions with its milieu. Only through those anatomical attributes can an individual possess consciousness [7].

When a child attempts its first step, prior attainment of the balanced upright position will have involved failed attempts, with attendant pain. What leads to discomfort will have been stored as memory of possible sensory feedback resulting from certain self-paced movements. Likewise, the fact that specific muscular movements can achieve forward motion will already be part of a repertoire accessible unconsciously. Ultimately, the child hits upon the correct combination and timing of elemental movements and the first successful step is taken. That consolidation into a more complex motor pattern is temporarily deposited in explicit memory [8], and subsequently transferred to long-term implicit memory [9], probably during the frequent periods of sleep [10,11], characteristic in infancy. Soon, the toddler is able to walk without concentrating on every step, and more complicated foot-related scenarios will enjoy brief sojourns at the center of the explicit stage.

The system conjures up a simulated probable outcome of the intended motor pattern, and vetoes it if the prognosis is adverse. The simulated outcome lies below the threshold for actual movement, and the mimicking requires two-way interaction between the nervous system and the spindles [12,13] associated with the skeletal musculature, particularly when the muscles are already in the process of doing something else. The interplay provides the basis of sensation, this always being in the service of anticipation.

The bottleneck in sensory processing [14] arises because planning of movement is forced to avoid potential conflict between the individual muscles. Because we learn about the world only through our actual or simulated muscular movements, this is postulated to produce the unity of conscious experience. Intelligence then becomes a measure of the facility for consolidating elementary movements (overt or covert) into more complex motor patterns, while creativity is the capacity for probing novel consolidations of motor responses.

We can think without acting, act without thinking, act while thinking about that act, and act while thinking about something else. Our acts can be composite, several muscular patterns being activated concurrently, though we appear not to be able to simultaneously maintain two streams of thought. When we think about one thing while doing something else, it is always our thoughts, which are the focus of attention. This suggests that there are least two thresholds, the higher associated with overt movement and the lower with thought. Assuming that the signals underlying competing potential thoughts must race each other to a threshold [15], it may be highly significant that cortical and thalamic projections form no strong loops [16]. As mentioned earlier, the presence of strong loops could make overt movement too automatic. We can now add a second possible penalty; thoughts might otherwise establish themselves by default. One should note that overt movement and mere imagery-that is, covert preparations for movement, appear to involve identical areas [17].

Thoughts, according to this scheme, are merely simulated interactions with the environment, and their ultimate function is the addition of new implicit memories, new standard routes from sensory input to permit motor output or new optimized complex reflexes. The duality of routes could well underlie the interplay between explicit and implicit in brain function.

A major problem confronting those who would explain consciousness is its apparently multifarious nature and the attendant difficulty in an effective operational definition. We attach great significance to the provision of context-specific reflexes, as occurs when one is learning to walk.

The nature of primitive reflex development on both motor and cognitive function has been more extensively reviewed elsewhere [18]. There has been a correlation shown between retained primitive reflexes and delayed motor development in very low birth weight infants [19]. They noted that very low birth weight (VLBW) infants retained stronger primitive reflexes and exhibited a significantly higher incidence of motor delays than did full-term infants. They confirmed a high

incidence of motor delays among VLBW infants and demonstrated a clear association between retained reflexes and delayed motor development in VLBW infants. It is important to note that this was in the absence of any overt pathology in the brains of these children.

In another study [20] the relationship between extreme low birth weight infants, motor and cognitive development at one and at 4 years was studied. The authors observed a relationship between motor ability and cognitive performance. Their study investigated the association between movement and cognitive performance at one and 4 years corrected age of children born less than 1000g, and whether developmental testing of movement at one year was predictive of cognitive performance at four years. Motor assessment at both ages was performed using the neurosensory motor developmental assessment (NSMDA). Cognitive performance was assessed on the Griffith Mental Developmental Scale at one year and McCarthy Scales of Children's Abilities at four years. A significant association was found between NSMDA group classification at one year and cognitive performance at both one and at four years and between the subscales of each test. They also noted that group classification of motor development at one year was predictive of cognitive performance at four years and this was independent of biological and social factors and the presence of cerebral palsy.

In yet another study, [21] the relationship between a normal intact cerebellum and primitive reflexes was examined. Tonic labyrinth and neck reflexes were studied separately and in combination in the decerebrate cat before and after acute cerebellectomy. The investigators noted clear changes in these reflexes both before and after surgery. They concluded that the presence of the cerebellum is required for the occurrence of the normal asymmetric labyrinth reflexes. Decreased size and immaturity as well as dysfunction of the cerebellum and the inferior olive are seen in almost all children with neurobehavioral disorders and these factors are thought to play a critical role in the development of normal coordination and synchronization of the motor system and the brain [2,11].

Romeo and associates [22] examined the relationship between the acquisition of independent walking. They noted that most of the infants they examined had a twostep development pattern. The infants at first showed an incomplete and then a complete FPR, which was observed more frequently at nine months. An incomplete FRP only, without successive maturation to a complete FPR was present in 21% of the whole sample. Infants with a complete FPR walked at a median age of 13 months, whereas those with an incomplete FPR only walked at a median age of 14 months. The investigators observed, in those with incomplete pattern, a trend toward delayed acquisition of independent walking.

Teitelbaum and associates [23] hypothesized that movement disturbances in infants can be interpreted as "reflexes gone astray" and may be early indicators of autism. They noted that in the children they reviewed, some had reflexes that persisted too long in infancy, whereas others first appeared much later than they should. The asymmetric tonic neck reflex is one reflex that they

noted may persist too long in autism. Head verticalization in response to body tilt they noted is a reflex that does not appear when it should in a subgroup of "autistic-to-be" infants They suggested that these reflexes may be used by pediatricians to screen for neurological dysfunction that may be a markers for autism.

Recovery Recapitulating Phylogeny as a Basis for Therapeutic Strategy in both Adults and Children

There are numerous consistencies between the successive developmental stages and recovery from brain injury. Hines (1942) had long ago demonstrated that the normal development of locomotion and posture in rhesus monkeys passed through states similar to those seen during stroke recovery. Teitelbaum et al. [24] found that the four stages of feeding behavior in normal development re-emerged in rats recovering from a lateral hypothalamic injury. Other studies from his laboratory determined that forelimb placing in the cat passed through the same stages during normal development and during recovery from a focal lesion [25]. Morerecent studies in humans lend further support to such a link, especially with regard to motor function. In other cases, such as language, the case for a parallel between development and recovery might be less compelling.

A major theme common to both childhood development and successful recovery from hemiparetic stroke or trauma is the refinement in motor performance, from a gross movement to a fractionated one, such as alexia without agraphia and a color naming deficit [26] where a person with brain damage could no longer read but could write and not be able to read what he wrote. The sequence of events after stroke was well described in the 1950s by Twitchell [27]. Initially, activity depends on reflex responses. Primitive reflexes are disinhibited. The first volitional movements consist of whole-arm synergistic events, then proximal movements predominate. Movement of individual fingers appears later, as synkinesias resolve, and only when recovery is substantial. Slowness of fine finger movements is a cardinal sign of corticospinal tract damage; faster movements and shorter reaction times are seen as stroke recovery proceeds. This general pattern is similar to motor changes during normal development. Newborn infants respond in a generalized fashion to stimulation, with early responses showing much more movement of the entire upper extremity rather than of individual fingers [28]. Over time, movements become more precise and fractionated, with loss of synkinesias and inhibition of primitive reflexes.

What are the changes in brain function that underlies these improvements in motor function during stroke recovery, and how similar are they to the events of normal development? Brain-mapping studies have provided some insights, and a number of similarities have emerged, including those related to bilateral motor control and those related to plasticity of cortical representational maps.

Bilateral Motor Control

Childhood is associated with bilateral motor control, in association with immaturity of the

corticospinal connections essential for fractionated unilateral movements. In contrast, adulthood is associated primarily with contralateral motor control, together with well-developed corticospinal tract size and function [29]. Muller et al. (1997) found that transcranial magnetic stimulation of motor cortex induced bilateral responses in hand and arm muscles of most children, but only contralateral responses from the age of ten. The frequency with which ipsilateral responses were seen steadily decreased during the first decade of life. Another indication of bilateral control is the movement of both hands during intended use of only one, a phenomenon known as mirror movements. Mirror movements during hand motor tasks are normal in children, but decrease in their prevalence and magnitude, then disappear in the early teenage years13. There are limited data that describe functional brain activation in children. Studies using near-infrared spectroscopy in normal infants have identified bilateral sensorimotor cortex activation during unilateral passive arm movements [30] in contrast to contralateral activation in response to the same movements in adults [31].

Gaillard et al. [32], using functional magnetic resonance imaging (fMRI) during a silent word-generation task, found that children activated a significantly larger volume of brain in the right hemisphere and in the right inferior frontal gyrus, when compared with adults. Bilateral motor control has also been described in adults who have suffered a stroke. Neurophysiological features, however, suggest two different patterns. One is found in individuals with poor motor status, either soon after stroke or late after stroke in individuals with poor recovery. Neurophysiological evaluation of these individuals discloses features in common with children. A second pattern of bilateral motor control has been described in individuals with good recovery after stroke and has more similarities with the normal adult motor physiology.

Soon after stroke, and in individuals with poor recovery long after stroke, studies have demonstrated an increased degree of bilateral motor control that has similarities with normal childhood motor function. A PET study of six hemiplegic individuals early after stroke found bilaterally increased sensorimotor cortex activation during passive movement of the paretic arm, when compared with the same stimulus in controls [33]; this is the same stimulus that produced bilateral sensorimotor cortex activation in infants and contralateral activation in healthy adults [34]. In the stroke hemisphere, soon after stroke and in individuals with poor recovery from stroke, there is often slowed central motor conduction time, a finding also seen in early childhood. In the non-stroke hemisphere, transcranial magnetic stimulation (TMS) elicits motor responses in the ipsilateral (stroke-affected) hand, primarily in individuals with poor motor status 19,20; such ipsilateral responses to TMS are seen in children but not in adults. Furthermore, these ipsilateral responses to TMS among individuals who have not recovered from a stroke are delayed by several milliseconds compared with contralateral responses, similar to results in children. As with motor behavior, neurophysiological characterization of individuals with poor motor status after stroke has a number of similarities with early stages of development.

Individuals with good recovery from a hemiparetic stroke also show increased bilateral motor control, however neurophysiological features are more consistent with findings in normal adults rather than a return to an early developmental pattern. PET and fMRI studies of individuals with good recovery after stroke have described bilateral activation in motor cortex regions during performance of a hand motor task [35,36]. In contrast to individuals with poor recovery, however, those who are well-recovered have normal central motor conduction times [37] and fail to demonstrate ipsilateral motor responses during TMS of the non-stroke hemi- sphere (as do control subjects) [38,39]. Numerous studies have found that control subjects performing a unilateral motor task recruit ipsilateral motor cortex, though to a smaller extent than stroke subjects moving a recovered hand [35,36,40]. The site of ipsilateral motor cortex recruited by stroke and control subjects is similar. In controls, the sites activated in a given hemisphere during ipsilateral and during contralateral hand movements are spatially distinct. In the nonstroke hemisphere of stroke subjects, the site activated during ipsilateral (recovered) hand movement is separated from the site activated during contralateral (unaffected) movement. The pattern of separation in stroke is very similar to that seen in controls [41], suggesting that in stroke, a cortical region normally used for movement is being recruited, but in an exaggerated way.

The role played by motor cortex in its influence on ipsilateral hand movements can vary according to the pattern of bilateral control. In the first pattern, seen in children and in are individuals who have suffered a stroke without good recovery, ipsilateral control of hand movements has been considered a reflection of activity in un-decussated corticospinal pathways [38,39]. The second pattern is seen in adults and in individuals with good recovery, suggesting that stroke recovery reflects reinstatement of motor control features that were acquired during development. In this group, ipsilateral control might reflect task complexity, as increasing the complexity of unilateral hand movements by normal adult subjects has been associated with greater activation of the ipsilateral motor cortex [42].

Cortical-Map Plasticity

Brain-mapping studies have supported the idea that in humans, a number of cortical regions contain orderly but overlapping representation of body regions [43]. In animal studies, these maps show a degree of redundancy and overlap, a finding also described in human brain- mapping studies [44]. The capacity to reorganize cortical representational maps might be maximal at early time points in development. For example, hemispherectomy during early childhood can be associated with remapping of motor, language and other functions to regions within the remaining hemisphere [6,45].

Multiple rearrangements can occur after a single stroke, and an improved understanding of cortical reorganization in this setting might come from studying patterns of change in multiple systems. For example, compared with controls, an individual recovered from a small precentral gyrus stroke showed a posterior shift in the activation site during both finger-motor and finger-

sensory paradigms [46]. The total behavioral impact of these reorganizational events is difficult to know. Gains in one aspect of function might arise at the cost of another; for example, this might explain why stroke subjects often have mild motor deficits in the nonstroke hand in association with improvement in the stroke-affected hand [35].

Evidence from animal and from human studies suggests that treatments targeting brain based rehabilitation must be linked with physical activity for benefits to be realized [5,18]. For example, a dramatic improvement in recovery is seen when rats with an experimental stroke are given amphetamine; if the drug is not paired with physical activity, however, this improvement was abolished [47]. Similarly, physical restraint can reduce post-stroke neuronal responses and impede recovery [48]. Such a bi-directional relationship between behavioral experience and brain structure during development has long been appreciated and might be of value in clarifying physiotherapy in relation to post-stroke molecular therapies.

Localization, Optimization and Connectivities as a Basis for Cognitive Rehabilitation

A neuroanatomical conceptualization based on localized function is largely an irrelevancy for cognitive rehabilitation in developmental disabilities both in childhood and adulthood. Our concern is not which brain area controls a given cognitive function, but how efficiently brain regions cooperate with each other. The reader is invited to review these concepts more comprehensively elsewhere [18,45].

Figure 1 presents a traditional view of the localization of language function in the adult brain and Figure 2 represents the nature of network processing of language not circumscribed to a particular locale but rather to an organization of networks for optimized performance. Figure 3 then takes the understanding of network processing and demonstrates a non-localized view of language processing.

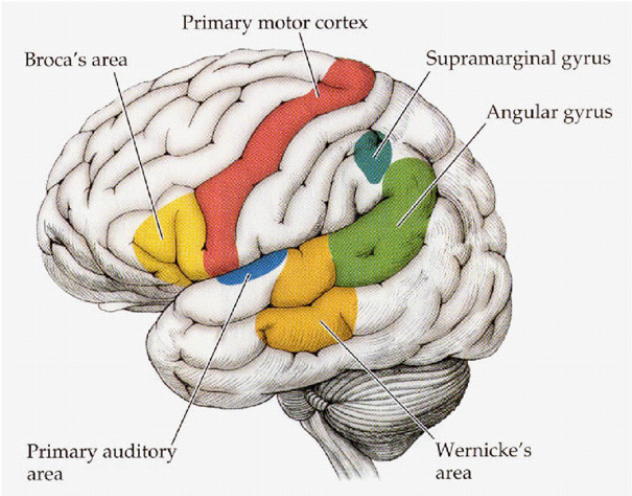

Figure 1: Traditional understanding of localization of language in adults.

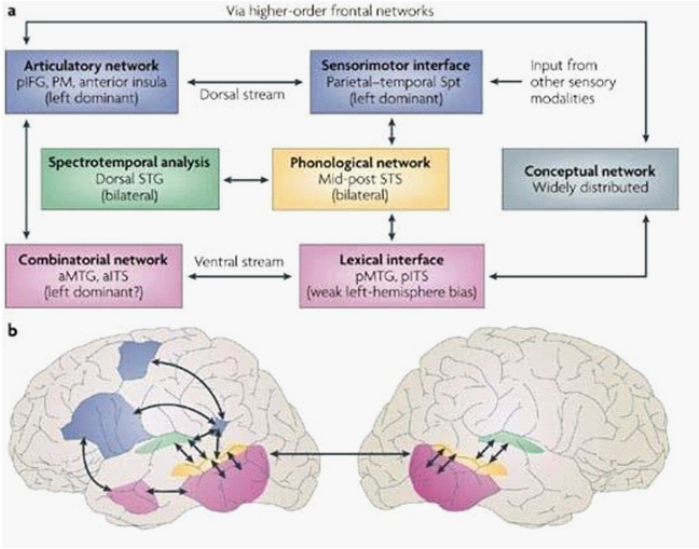

Figure 2: Multiple stream models of receptive language functions organized into multiple self-organizing simultaneously active networks [49].

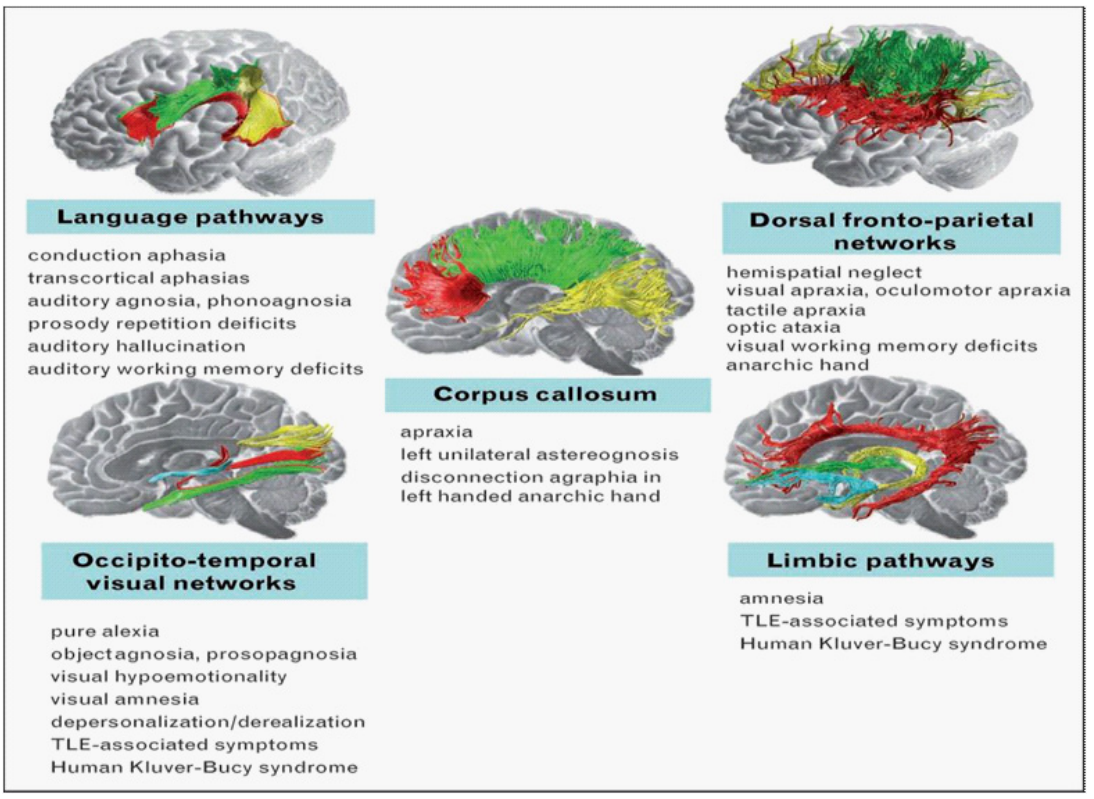

Figure 3: Functional cortical networks measured by tractography [50].

A concept of ''cortical efficiency'' [51-53] indicates that higher ability in a cognitive task is associated with more efficient neural processing and not necessarily a particular brain region that is involved in that processing. Intuitively, we would expect higher performance to correlate with more activity, for the cerebral cortex the contrary is the case. Higher performance in several tasks, including verbal [54], numeric, figural, and spatial reasoning [55,56] is consistent with the reduced consumption of energy in several cortical areas.

This phenomenon has also been studied with EEG techniques in different frequency bands. The function of childhood neurological development is precisely to facilitate the creation of localized function and it is dynamic. It can be changed and is therefore plastic. This localization of function is not the explanation of a process, but rather the end-result of training. The efficiency of cognitive function is directly a consequence of the effectiveness of networks that now can be measured. Fewer brain regions necessary to accomplish a single task in one individual compared to another for the same task is a measure of efficiency.

These networks, active during learning and problem solving of all kinds, are plastic and can be changed as a direct consequence of experience and training. In attempting to apply graph theory concepts to child and adolescent neurocognitive performance to create a fundamental change in the educational training and evaluation paradigm, we can characterize the organization & development of large-scale brain networks using graph-theoretical metrics as represented in Figure 4 below.

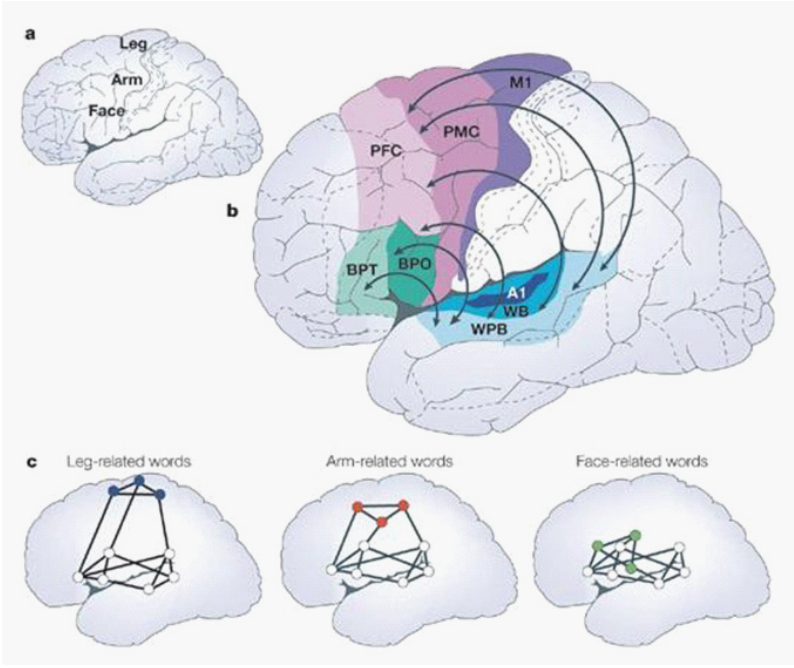

Figure 4: Grounded meaning indicates that the meaning of words and sentences are "embodied" [57].

Motor-Cognitive Relationships in the Justification of Cognitive Rehabilitation

Although there exist numerous definitions of intelligence beyond one's ability to perform on intelligence tests, it is possible to define intelligence operationally as, "the ability to consolidate already-learned motor patterns into more complex composites, such consolidation sometimes being merely covert, rather than overt." This definition was discussed in the context of autism [18]. A normal child, lying on its back and wanting to roll over onto its front, soon learns that this can be readily accomplished if first the head, then the shoulders, and finally the hips are swiveled in the same direction. If the timing of this sequence is correct, the supine-prone transition requires a minimum of effort. Autistic infants appear to experience considerable difficulty in learning this simple motor sequence. Indeed, the sequence does not even occur in their failed attempts. Instead, they awkwardly arch their backs and ultimately fall into the desired position.

When a new motor pattern is being acquired, both the means and the ends will be coded in currently active patterns of neuronal signals. And there must be interactions between these patterns because the goal will influence the route through muscular hyper- space by which it is to be achieved. The prefrontal cortex probably dictates patterns of elementary muscular sequences, but it must be borne in mind that the sophistication of the latter will depend upon what the individual has already learned. A ballet dancer would regard as an elementary motor pattern a muscular sequence, which the novice would find quite difficult. The most spectacular feature to evolve thus far has been that seen in the mammals, and it permitted acquisition, during a creature's own lifetime, of novel context-specific reflexes, especially those relying on sequences of muscular movements. This mechanism makes heavy demands on the neural circuitry, because it requires an attentional mechanism. As attention must be an active process, there must be feedback from the muscles, carrying information about their current state, including their current rate of change of state. Without such information, anticipation would be impossible, and without anticipation there could be no meaningful adjudication and decision as to the most appropriate way of continuing an on-going movement. Without such a mechanism, novel context specific reflexes could not be acquired.

The fascinating thing is that access to such on-line information mediates consciousness, the gist of which is the ability to know that one knows. The ability to know that one knows is referred to by psychologists as first-order embedding. Higher embedding, such as that exemplified by knowing that one knows that one knows, merely depends upon the ability to hold things in separate patches of neuronal activity in working memory. This manifests itself in a creature's intelligence, which also dictates its ability to consolidate existing schemata into a new schema. When we know that we know, the muscular apparatus is not only monitoring its own state, it is monitoring the monitoring.

It is precisely this absence of anticipation that impedes the ability of the brain injured to

recover and why it is that the discussion of the early development and the discussion of primitive reflexes become highly relevant in justifying programs of cognitive rehabilitation. The return of primitive reflexes and the impairment of linkages between motor and cognitive function learned early in life must be relearned.

In short, one can think of the overall influence of the motor system on the frontal cortex as "releasing the brakes" for motor actions and other functions.

THERAPEUTIC THEORY AND STRATEGY

At first glance, the answer to how intervention strategies should be developed seems simple - increase stimulation and provide the proper fuel. The attempt should be to relearn the motor and cognitive tasks associated with the decrease and disappearance of primitive reflexes seen in the developing child and reappearing in the neurologically compromised adult. In practice, however, it is not quite that straightforward. The purpose of this chapter is to provide the theoretical rationale for therapeutic and intervention strategies currently available, but not to provide a "how to" manual, the subject of a subsequent volume. We need now to consider how we increase stimulation and what could be the best fuel.

Treatment Rationale

The current thinking is that only two options for treatment exist: one being medication and physical interventions which makes up approximately 75 percent of recommendations and the other being psychological or behavioral counseling including neuropsychology which makes up the other 25 percent. Numerous alternative effective treatment options are available and discussed in the context of recent brain, behavioral, pharmacological, biochemical, and genetic research.

Behavioral Intervention Strategies

Cognitive behavioral therapy

This form of therapy has been used on adults for many fears or *phobias, anxiety disorders, panic attacks, and post traumatic stress disorder*. Developed in the 1960's by psychiatrist Aaron Beck (1967,1976), this form of therapy gradually allows those with these disorders to talk about, physically approach, and ultimately experience the very things that terrify them. It is thought that this particular form of therapy deliberately sets up a program of repeated programmed self-awareness exercises to rewire connections in the brain and form helpful new memories, just as repetitive practicing of the piano gradually creates a memory of motor skills. Common cognitive distortions without a neurobehavioral disorder likely have adaptive evolutionary value. Cognitive distortions are natural consequences of using fast track defensive algorithms that are sensitive to threat. In various contexts, especially those of threat, humans have evolved to think adaptively rather than logically. Hence, cognitive distortions are not strictly errors in brain functioning and it can be useful to inform patients that 'negative thinking' may be dysfunctional but is a reflection

of basic brain design and not personal irrationality. The neuropathology underlying ADHD and neurobehavioral disorders in general most consistently points to dysfunction in cortical-striatal pathways leading to inactivation, or insufficient engagement, of frontal and prefrontal lobes. By implication, there may be functional disconnection between the anterior and posterior higher cortical regions, instead of a fixed dysfunction in either one. Given this premise, reconnection of these systems via cognitive interventions constitutes a logical remedial approach in the treatment of ADHD and neurobehavioral disorders through integrative cognitive and neuropsychological interventions.

Related to neurobehavioral disorders, however, studies have shown that CBT is just as effective as drugs in many instances [58,59]. Rosenberg and colleagues [60] had studied the pathophysiology of obsessive-compulsive disorder treated by CBT. They had reported increased thalamic volume in treatment-naive pediatric OCD patients versus case-matched healthy comparison subjects that decreased to levels comparable to control subjects after effective paroxetine therapy. No study prior to theirs had measured neuro-anatomic changes in the thalamus of OCD patients near illness onset before and after CBT. Volumetric magnetic resonance imaging studies were conducted in 11 psychotropic drug-naive 8-17-year-old children with OCD before and after 12 weeks of effective CBT monotherapy. They reported no significant change in thalamic volume in OCD patients before and after cognitive behavioral therapy suggesting that reduction in thalamic volume after paroxetine therapy may be specific to paroxetine treatment and not the result of a general treatment response or spontaneous improvement. However, recent research has demonstrated that CBT for OCD can systematically modify cerebral metabolic activity in a manner, which is significantly related to clinical outcome. There does exist a substantial body of research supporting an involvement of neural circuitry connecting the orbitofrontal cortex, cingulate gyrus, and basal ganglia in the expression of the symptoms of OCD. Data has been reported [61] which expands upon previous work demonstrating effects of CBT on functional interactions between limbic cortex and the basal ganglia reflecting the interactive nature of the relationships between cognitive choice, behavioral output and brain activity.

Cognitive behavioral therapy gradually stimulates the neocortex by increasingly having the patients physically interact with their environment. We have seen that children exposed to violence or neglect have similar symptoms as posttraumatic stress disorder, where the amygdala and limbic system are overactive. In children, this results from a delayed development of the prefrontal cortex and the amygdala remains the primary site of emotionally based information processing. The rise of physical activity engages the muscle and joint receptors and the cerebellum, which is the initiator of all human learning, cognitive or social. The cerebellum also is the largest source of stimulation to the thalamus and the prefrontal cortex as well as the basal ganglia. As the person physically interacts with the environment, it induces the cerebellum to promote developments of the prefrontal cortex, which then inhibits the amygdala and limbic system, which reduces the fear and stress responses. The prefrontal cortex now allows the individual to have perception

that is more appropriate and awareness of the reaction of others to their actions as they learn what is socially appropriate behavior. We also think that the recall the painful memories at the same time helps to link these in time and space or synchronize these memories with other areas, if the now more efficiently functioning neocortex forms new associative cognitive patterns for the previously inhibited emotions. The individual would be theoretically forming new memories that are less disturbing than the previous associations.

Wykes and colleagues [62] had performed an evaluation of the effects on the brain of cognitive behavioral therapy (CBT) by means of functional magnetic resonance imaging (fMRI). The authors examined the effects on brain activity as a result of engaging in cognitive behavioral therapy. Three groups (patients receiving control therapy or cognitive behavioral therapy and a healthy control group) were investigated in a repeated measures design using the two-back test. Data obtained by fMRI and a broad assessment of executive functioning was completed at baseline and post-treatment. Brain activation changes were identified after accounting for possible task-correlated motion artifact. The fMRI analyses indicate that the control group shows decreased activation but the two patient groups show significant increases in activation over time. The patient group that receives successful cognitive behavioral therapy has significantly increased brain activation in regions associated with working memory, particularly the frontal cortical areas. The results are the first ever indications that brain activation changes in a seriously disabled group of patients with schizophrenia can be associated clearly with psychological rather than pharmacological therapy.

A study was performed in which the effects of citalopram and CBT on regional cerebral blood flow (rCBF) were explored in social phobia by means of positron emission tomography (PET) [63]. rCBF was assessed in 18 previously untreated patients with social phobia during an anxiogenic public speaking task. Patients were matched for sex, age, and phobia severity, based on social anxiety questionnaire data, and randomized to citalopram medication, CBT group therapy, or a waiting-list control group. Scans were repeated after 9 weeks of treatment or waiting time. The outcome was assessed by subjective and psychophysiological state anxiety measures and self-report questionnaires. The questions were re-administered after one year. The results indicate that symptoms improved significantly and roughly equally with citalopram and CBT, whereas the waiting-list group remains unchanged. Within both treated groups, and in responders regardless of treatment approach, improvement is accompanied by a decreased rCBF-response to public speaking bilaterally in the amygdala, hippocampus, and the periamygdaloid, rhinal, and parahippocampal cortices. Between-group comparisons confirm that rCBF in these regions decreases significantly more in treated groups than in control subjects, and in responders than non-responders, particularly in the right hemisphere. The degree of amygdala-limbic attenuation is associated with clinical improvement a year later. The authors conclude that common sites of action for citalopram and CBT of social anxiety are observed in the amygdala, hippocampus, and neighboring cortical areas that subserve bodily defense reactions to threat.

CBT can be employed as a systematic effort to assist brain impaired individuals in developing ways to compensate for cognitive deficits. Brett and Laatscha [64] had evaluated children with acquired nervous system brain injury receiving biweekly CBT sessions for 20 weeks in a school setting. Treatments were provided by trained schoolteachers under the supervision of psychologists specializing in cognitive rehabilitation. Students were evaluated pre- and posttreatment using neuropsychological tests. After treatment, the students demonstrated a significant increase in general memory ability. These gains were due mostly to increases in verbal learning ability according to the authors. The theoretical rationale for CBT intervention has been practically adapted to attempt to teach meta-cognitive executive thinking strategies to children with disorders of executive function. The intervention is based on the notion that some children with disorders of executive function have disorders of higher-level language, which predispose them to the executive impairments demonstrated. The teaching and reinforcing of meta-cognitive thinking strategies may well help advance verbal mediation of complex tasks and selfregulation of behavior in children with neurobehavioral disorders. Despite the growing literature on developmental executive disorders, little has been written about interventions that may enable the children to acquire some of the requisite adaptive skills.

Utilizing performance on intelligence testing spanning 20 years, Bellus and colleagues [65] performed a study evaluating changes in cognitive functioning of a severely brain injured individual, who had been placed in a long-term psychiatric hospital and treated in an intensive behavioral rehabilitation program. Results found that the patient demonstrated a significant improvement in overall verbal and nonverbal cognitive functioning during treatment. These improvements were maintained for a 1-year period. The authors suggest that the use of 'low tech', small group interventions, within intensive behavioral rehabilitation programs, may lead to the recovery of cognitive functioning for individuals who are significantly cognitively and socially impaired. Applying the same rationale to children with acquired brain injury and with difficulties in problem solving and social adjustment, Suzman and associates [66] provided case studies and a series of multiple baseline experiments examining the effects of a multi-component CBT on the remediation of problem solving deficits in five children with acquired brain injury. Results indicate that the training program resulted in a substantial decrease in errors on a computerized problem-solving task used to monitor problem-solving performance during baseline and treatment. In addition, significant improvements are found on two of four standardized measures of problem solving abilities.

Frolich and associates [67] have indicated that in the past, cognitive behavioral treatment concepts failed to demonstrate their clinical effectiveness in the treatment of ADHD children. They combined CBT with a special focus on selfinstructional and self-management skills with subsequent parent management training PMT in order to reduce academic problems and oppositional/aggressive behavior. Eighteen children with a diagnosis of ADHD combined type and Oppositional Defiant Disorder participated in the study. The effects of a 12-week treatment

phase (6 weeks CBT; 6 weeks PMT) were compared with a preceding 4-week baseline. Core symptoms of ADHD, conduct, and homework problems were assessed by weekly administration of parent and teacher questionnaires. CBT was found effective in reducing the core symptoms of ADHD and conduct problems at home and in school. PMT resulted in a further amelioration of the cited symptoms. These investigators conclude that CBT is an important component in the treatment of ADHD if aspects of generalization are considered. PMT is a useful adjunct to CBT due to its effectiveness in situations where children still have problems of self-guidance.

Stevenson and colleagues [68] attempted to systematically examine the efficacy of a CBT for management of adult Attention Deficit Hyperactivity Disorder (ADHD). Their CBT program was designed to target problems commonly associated with adult ADHD, namely, attention problems, poor motivation, poor organizational skills, impulsivity, reduced anger control, and low self-esteem. In a randomized, controlled trial, a representative sample of adults with ADHD who were both medicated and non-medicated were assigned to either CBT or a waiting list control. CBT was delivered in an intensive format with eight two-hour, weekly sessions with support people who acted as coaches, and participant workbooks with homework exercises. Participants who completed CBT reported reduced ADHD symptoms, improved organizational skills, and reduced levels of anger. Clinically significant improvements in ADHD symptoms and organizational skills were maintained one year after the intervention. The study's authors conclude that the CBT provides a practical way of enhancing daily functioning for adults with ADHD.

Wilmshurst [69] examined youth with severe emotional and behavioral disorders (EBD) by randomly assigning them for 3 months of intensive treatment to a 5-day residential program or a community-based alternative, family preservation program. Programs differed not only in method of service delivery (residential unit vs. home-based), but also in treatment philosophy (solution focused brief therapy vs. CBT. Results confirm high rates of comorbidity in this population for externalizing and internalizing disorders. A significant Treatment x Program interaction was evident for internalizing disorders. At 1-year follow-up, significantly higher percentages of youth from the family preservation program revealed a reduction of clinical symptoms for ADHD, as well as, general anxiety and depression, whereas significant proportion of youth from the 5-day residential program demonstrate clinical deterioration and increased symptoms of anxiety and depression. These investigators conclude that greater emphasis be placed on research linking treatment to specific symptom clusters, especially highly comorbid clusters based on neuropsychological test performance.

Eye Movements as Reflective of Neurococognitive Processes Employed in Behavioral Therapeutic Intervention

Our eyes usually move in brief motions called saccades. Between the saccades, they focus on the objects that we see [70]. Although our eyes move several times per second, we perceive the world only during the brief movements of fixation [70]. In essence, we can think of our visual

experience as a rapid sequence of still life photographs. However, the fixations occur too rapidly for us to notice the interval between the snapshots [70].

The saccadic eye movements, generated during a visual oddball task, of autistic children, normal children, children with attention deficit hyperactivity disorder (ADHD), and dyslexic children were examined to determine whether autistic children differed from these other groups in saccadic frequency [71]. Autistic children made more saccades during the presentation of frequent stimuli (than normals and ADHD children), and between stimulus presentations. In addition, unlike the normal and dyslexic groups, their saccadic frequency did not depend on stimulus type. This abnormal pattern of saccades may negatively influence the ability to attend to stimuli, and thereby learning processes.

Goldberg and colleagues [72] employed ocular-motor paradigms to examine whether or not saccades are impaired in individuals with high functioning autism (HFA). They recorded eye movements in patients with HFA and in normal adolescents on anti-saccade, memory-guided saccade MGS, predictive saccade, and gap/overlap tasks. Compared with the normal subjects, patients with HFA had a significantly higher percentage of directional errors on the anti-saccade task, a significantly higher percentage of response suppression errors on a MGS task, and a significantly lower percentage of predictive eye movements on a predictive saccade task. They also showed longer latencies on a MGS task and for all conditions tested on a gap/null/overlap task (fixation target extinguished before, simultaneously, or after the new peripheral target appeared). When the latencies during the gap condition were subtracted from the latencies in the overlap condition, there was no difference between patients and normals. These authors conclude that abnormalities in ocular motor function in patients with HFA provide evidence for the involvement of a number of brain regions in HFA including the dorsolateral prefrontal cortex, the frontal eye fields, the basal ganglia, and parietal lobes.

It is known that autistic children demonstrate abnormal gaze behavior toward human faces as observed in daily-life situations [73-75]. Van der Geest and associates [74] investigated this process in two fixation time studies. They selected a group of high-functioning autistic children (including a group of sub-threshold PDD-NOS children) who were compared with a group of normal children, with respect to their fixation behavior for photographs of human faces. Using an infrared eye-tracking device, fixation times for the whole face and for the facial elements of faces were compared between the two groups. The first study dealt with faces having an emotional expression. The second study dealt with neutral faces presented either upright or upside-down. Results indicated that autistic children have the same fixation behavior as normal children for upright faces, with or without an emotional expression. Furthermore, results of the second study showed that normal children spent less time looking at upside-down faces, but that the fixation times of autistic children were not influenced by the orientation of the faces. These results plead against the notion that the abnormal gaze behavior in everyday life is due to the presence of facial stimuli per se. Furthermore, the absence of a face orientation effect in autistic children might be

a reflection of a lack of holistic processing of human faces in autism and is a problem that may be addressed by therapeutic intervention using eye movements.

Van der Geest and associates [75] additionally noted that autistic children have a problem in processing social information and that that several studies on eye movements have indeed found indications that children with autism show particularly abnormal gaze behavior in relation to social stimuli even though previous studies did not allow for precise gaze analysis. In the their study [75], the looking behavior of autistic children toward cartoon-like scenes that included a human figure was measured quantitatively using an infrared eye-tracking device. The fixation behavior of autistic children was found to be similar to that of their age- and IQ-matched normal peers. Their results do not support the notion that autistic children have a specific problem in processing socially loaded visual stimuli as reflected by eye tracking. In addition, there is no indication for an abnormality in gaze behavior in relation to neutral objects. It is suggested that the often-reported abnormal use of gaze in everyday life is not related to the nature of the visual stimuli but that other factors, like social interaction. Therefore, intervention strategies employing eye movements as a therapeutic vehicle are theoretically useful.

These same investigators [73] hypothesized that children with autism have deficits in attentional (dis-) engagement mechanisms. A saccadic gap-overlap task was used to study visual engagement and disengagement in 16 high-functioning autistic children of about 10 years of age and 15 age- and IQmatched normal control children. Subjects were asked to make saccadic eye movements from a fixation point to a suddenly appearing target as fast as possible. The saccadic reaction time was compared in two conditions: 1) the overlap condition, in which the fixation point was continuously visible, and 2) the gap condition, in which the fixation point was turned off 200 msec. before the target appeared. Although no differences between the groups in either condition was observed, the gap effect (i.e., the difference in saccadic reaction time between the overlap condition and the gap condition) was smaller in the autistic group than in the control group. They concluded that autistic children show a lower level of attentional engagement.

Ruffman and colleagues [76] addressed these issues by studying social understanding in autism employing eye gaze as a measure of core insights. Twentyeight children with autism and 33 mentally handicapped children were given two tasks tapping social understanding and a control task tapping probability understanding. For each task, there was a measure of eye gaze (where children looked when anticipating the return of a story character or an object) and a verbal measure (a direct question). They found that eye gaze was better than verbal performance at differentiating children with autism from children with other mental handicaps. Children with autism did not look to the correct location in anticipation of the story character's return in the social tasks, but they did look to the correct location in the nonsocial probability task. These investigators also found that within the autistic group, children who looked least to the correct location were rated as having the most severe autistic characteristics. Further, they found that whereas verbal performance correlated with general language ability in the autistic group, eye

gaze did not. They argue that eye gaze probably taps unconscious but core insights into social behavior and as such is better than verbal measures at differentiating children with autism from mentally handicapped controls. Additionally, eye gaze taps either spontaneous processes of simulation or rudimentary pattern recognition, both of which are less based in language, and the social understanding of children with autism is probably based mostly on verbally mediated theories whereas control children also possess more spontaneous insights indexed by eye gaze.

Manifestations of core social deficits in autism are more pronounced in everyday settings than in explicit experimental tasks. To bring experimental measures in line with clinical observation, Klin and associates [77] reported a novel method of quantifying atypical strategies of social monitoring in a setting that simulate the demands of daily experience. While viewing social scenes, eye-tracking technology measured visual fixations in 15 cognitively able males with autism and 15 age-, sex-, and verbal IQ-matched control subjects. The investigators coded fixations on 4 regions: mouth, eyes, body, and objects. Statistical analyses compared fixation time on regions of interest between groups and correlation of fixation time with outcome measures of social competence (i.e., standardized measures of daily social adjustment and degree of autistic social symptoms). They found significant between-group differences for all 4 regions with the best predictor of autism being reduced eye region fixation time. Fixation on mouths and objects was significantly correlated with social functioning: increased focus on mouths predicted improved social adjustment and less autistic social impairment, whereas more time on objects predicted the opposite relationship. When viewing naturalistic social situations, individuals with autism demonstrate abnormal patterns of social visual pursuit consistent with reduced salience of eyes and increased salience of mouths, bodies, and objects. Fixation times on mouths and objects but not on eyes are strong predictors of degree of social competence.

From an evolutionary standpoint gaze is an important component of social interaction. The function, evolution, and neurobiology of gaze processing are therefore of interest in the context of neurobehavioral disorders of childhood. The role of social gaze has changed considerably for primates compared to other organisms. This change may have been driven by morphological changes to the face and eyes of primates, limitations in the facial anatomy of other vertebrates, changes in the ecology of the environment in which primates live, and a necessity to communicate information about the environment, emotional and mental states. The eyes represent different levels of signal value depending on the status, disposition, and emotional state of the sender and receiver of such signals. There are regions in the monkey and human brain, which contain neurons, that respond selectively to faces, bodies, and eye gaze. The ability to follow another individual's gaze direction is affected in individuals with autism and other neurobehavioral disorders as we have seen, as well as following particular localized brain lesions. We can hypothesize that gaze following is "hard-wired" in the brain, and may be localized within a circuit linking the superior temporal sulcus, amygdala, and orbitofrontal cortex. A more complete review is provided by

Emery [78]. This being the case the with developmental neurobehavioral disorders should clearly be involved in intervention strategies employing eye gaze as a vehicle.

Supporting the notion of eye gaze involvement, Howard and colleagues [79] reported a convergence of behavioral and neuroanatomical evidence in support of an amygdala hypothesis of autism. They found that high-functioning autistics (HFA) show neuropsychological profiles characteristic of the effects of amygdala damage, in particular selective impairment in the recognition of facial expressions of fear, perception of eye-gaze direction, and recognition memory for faces. Using quantitative magnetic resonance imaging analysis techniques, they found that the same individuals also show abnormalities of medial temporal lobe, notably bilaterally enlarged amygdala volumes. These results combine to suggest that developmental malformation of the amygdala may underlie the social-cognitive impairments characteristic of HFA. While they attribute these findings to incomplete neuronal pruning in early development, these data further support a primary underlying involvement of eye-gaze.

Eye movement dysfunction also is likely to occur after injury at several levels of the neuraxis. Unilateral supranuclear disorders of gaze tend to be transient, but bilateral disorders more enduring Nuclear disorders of gaze also tend to be enduring and are frequently present in association with long tract signs and cranial nerve palsies on opposite sides of the body. Nystagmus is a reliable sign of posterior fossa or peripheral eighth nerve pathology. Familiarity with these concepts may help the clinician answer questions regarding localization and prognosis and their remediation in post head injury insult or in developmental disorders is necessary.

Disturbances in the orbital prefrontal cortex and its ventral striatal target fields have been In attempting to explain further why gaze-shift impairment is part of the clinical picture in neurobehavioral disorders, we should recall that imaging and clinical studies have challenged the concept that the functional role of the cerebellum is exclusively in the motor domain. Townsend and associates [80] presented evidence of slowed covert orienting of visual-spatial attention in patients with developmental cerebellar abnormality (at least 90 percent of all postmortem cases of autism reported to date have Purkinje neuron loss), and in patients with cerebellar damage acquired from tumor or stroke. In spatial cuing tasks, normal control subjects across a wide age range were able to orient attention within 100 msec. of an attentiondirecting cue. Patients with cerebellar damage showed little evidence of having oriented attention after 100 msec. but did show the effects of attention orienting after 800-1200 msec. These effects were demonstrated in a task in which results were independent of the motor response. In this task, smaller cerebellar vermal lobules VIVII (from magnetic resonance imaging) were associated with greater attentionorienting deficits.

Although eye movements may also be disrupted in patients with cerebellar damage, abnormal gaze shifting cannot explain the timing and nature of the attentionorienting deficits. These data is consistent with evidence from organism models that suggest damage to the cerebellum disrupts both the spatial encoding of a location for an attentional shift and the subsequent gaze shift. These

data are also consistent with a model of cerebellar function in which the cerebellum supports a broad spectrum of brain systems involved in both non-motor and motor function identified in neuroimaging studies of obsessive-compulsive disorder (OCD). In animal models and studies of patients with lesions to this brain circuitry, a selective disturbance in the ability to suppress responses to irrelevant stimuli has been demonstrated. Such a deficit in response suppression might underlie the apparent inhibitory deficit suggested by the symptoms of OCD. Although OCD commonly emerges during childhood or adolescence, few studies have examined psychotropic-naive pediatric patients near the onset of illness to find the possible role of atypical developmental processes in this disorder. Ocular-motor tests were administered to 18 psychotropic medication-naive, non-depressed patients with OCD aged 8.8 to 16.9 years and 18 case-matched healthy comparison subjects to assess the following 3 well-delineated aspects of prefrontal cortical function: the ability to suppress responses, the volitional execution of delayed responses, and the anticipation of predictable events. A significantly higher percentage of response suppression failures were observed in patients with OCD, particularly in younger patients compared with their case-matched controls. No significant differences between patients with OCD and controls were observed on other prefrontal cortical functions. Severity of OCD symptoms was related to response suppression deficits. A basic disturbance of behavioral inhibition in OCD was detected that may underlie the repetitive symptomatic behavior that characterizes the illness [81].

Mostofsky and colleagues [82] assessed saccadic eye movements in boys with Tourette's syndrome with and without ADHD, comparing performance with that of an age-matched group of male controls. Three different saccade tasks (prosaccades, antisaccades, and memory-guided saccades) were used to examine functions necessary for the planning and execution of eye movements, including motor response preparation, response inhibition, and working memory. The study included 14 boys with Tourette's syndrome without ADHD, 11 boys with Tourette's syndrome and ADHD, and 10 male controls. Mostofsky and associates found that the latency of prosaccades was prolonged in boys with Tourette's syndrome (both with and without ADHD) compared with controls. Variability in prosaccade latency was greater in the groups of boys with Tourette's syndrome and ADHD compared with both the Tourette's syndrome-only and control groups. Response inhibition errors on both the antisaccade task (directional errors) and memory-guided saccade task (anticipatory errors) were increased in boys with Tourette's syndrome and ADHD compared with those with Tourette's syndrome-only. There were no significant differences among the three groups in accuracy of memory-guided saccades. Mostofsky's ocular-motor findings suggest that Tourette's syndrome is associated with delay in initiation of motor response as evidenced by excessive latency on prosaccades. Signs of impaired response inhibition and variability in motor response appear to be associated with the presence of ADHD.

Abnormalities of executive function are observed consistently in children with ADHD, and it is hypothesized that these arise because of disruption to a behavioral inhibition system. In examining contextual abnormalities of saccadic inhibition in children with attention deficit

hyperactivity disorder, Cairney and associates (2001). Executive and inhibitory functions were compared between unmedicated and medicated children with ADHD, age-matched healthy children and healthy adults. Executive functions were measured using a test of spatial working memory shown previously to be sensitive to ADHD and to stimulant medication. Inhibitory functions were measured using an ocular motor paradigm that required individuals to use task context to control the release of fixation. Context was set according to the probability that a target would appear at either of the two locations. In one block, targets appeared on 80 percent of trials. In the other block, targets appeared on 20 percent of trials. The ability to control the release of fixation was inferred from the fixation-offset effect, or the difference in saccade latency when the current fixation is offset 200 ms prior to the onset of the saccade target (gap condition), compared with when there is no offset (overlap condition). Although the healthy children made more errors on the spatial working memory task than the healthy adults, there was no difference between the two groups in their ability to control fixation, using context. Both showed a larger fixation-offset effect when target probability was low. The unmedicated ADHD group made more errors on the spatial working memory test than the healthy children, although spatial working memory performance was normal in the medicated ADHD group. However, both the unmedicated and medicated ADHD groups were unable to modulate the fixation-offset effect according to context, and this was due to their inability to voluntarily inhibit saccades when there was a low target probability. These data suggest that the context-based modulation of fixation release is not controlled by the same systems that control executive function. Furthermore, deficits in executive function and inhibitory control appear independent in children with ADHD with others [83,84] having found similar effects in both males and females.

Bergmann [85] speculated that the hippocampus and amygdala are involved in using eye movements as a rehabilitation tool. He notes that it is thought that these two structures are involved in much of the brains learning and remembering.

Therefore where the amygdala "retains the emotional flavor of memory, the hippocampus retains the dry facts." He also notes that inhibition of the amygdala is thought to arise from the left prefrontal cortex [86].

Sensory information from visual, auditory, olfactory areas bypasses the thalamus (indirect activity with thalamus) are first sent to the thalamus and then monosynaptically to the amygdala. A second pathway from the thalamus projects to the neocortex; this arrangement allows the amygdala to react before the neocortex. The neocortex processes the information through several brain circuits before it finally perceives and responds [86]. It has been suggested that eye gaze interventions resynchronizes the activity of the two hemispheres, by way of the alternating stimulus which may mimic the activity of the pacemaker function within the cortex that may be suppressed. Bergmann [85] concludes "stated more specifically, eye movement retraining gradually shifts the brain activity from amygdaline hyperactivity to activation of greater neocortical function."

Eye movement training can be powerful but difficult to perform for many children with learning or behavioral problems. Eye movement training that is more specific to the side of the cerebellar or cerebral deficit has been clinically found to be more effective. As children become more coordinated with their eye movements, there usually is improvement in learning and behavior. A direct neurological connection exists between the neck and extra-ocular muscles; examining for weakness and fatigability of eye muscles can test weakness of neck muscles. It has been noted that many children with neurobehavioral disorders have difficulty or cannot cross their eyes (convergence) in the midline [87]. The extraocular muscles are analogous to midline postural muscles, with weakness in each reflecting a bilateral limitation. The child may be able to adduct one eye and not the other, this usually represents a unilateral weakness or neurological imbalance, and the weakness is often found on the same side as a neocortical decrease in activation. Saccadic dysmetria especially hypometria is more indicative of cerebellar deficit. Saccadic dysmetria with the child looking up to the right or down and left is usually associated with right cerebellar lesions, whereas up and left and down and right dysmetria is associated with left cerebellar lesions. These findings need to be correlated with other signs and symptoms. There are currently some interesting studies examining eye movement intervention strategies in neurobehaviorally involved children using functional imaging techniques that should reveal or confirm more specifically it effectiveness and mechanism of function.

Biofeedback

Biofeedback training provides a tool to consciously control the autonomic nervous system using biofeedback devices in order to alleviate stress, migraine headaches, asthma, high blood pressure, and a host of other health conditions including epilepsy. Neurofeedback or EEG biofeedback is the form of biofeedback typically used on children with epilepsy and neurobehavioral conditions like hyperactivity, ADHD, learning disability, etc. It is also effective for cardiac arrhythmias employing cognitive means. It is thought that neurofeedback seems to work by interacting in the area of frequency of signal transmission. Frequency in this context is the rate at which electrical activity proceeds through the nervous system. EEG measures human brain activity in specific frequency ranges. These frequency ranges are reflective of states of consciousness and each frequency range is a component of a bounded continuum ranging from death through various states of sleep and ultimately to excitement and seizures. These are described in Table 1 and Figure 5 below:

Table 1: EEG Frequency Ranges

Waveform	Frequency Range (in Hz)	Amplitude (in μV)	Occurrence
Gamma rhythm	30-50		Excitement
Beta rhythm	18-30	< 10	Alert/eyes open, arousal, anterior scalp
Alpha rhythm	8-13	0-40	Adults, older children, relaxed wakefulness/eye closed, parietal, occipital temporal regions
Mu rhythm	7-11	0-20	Asymmetric, asynchronous between 2 sides at times unilateral, central parietal, attenuates with contralateral extremity movement, thought of movement, or tactile stimulation; no reaction to eye opening and closing
Theta rhythm	4-7	40-60	Childhood, light sleep, temporal areas through adolescence
Delta rhythm	0.5-4	40-200	Sleep
Delta rhythm	0.5-3	40-200	Infancy, deep sleep, coma
Lambda & K complex & sleep spindles	Not defined solely in terms of rhythm		Deep sleep

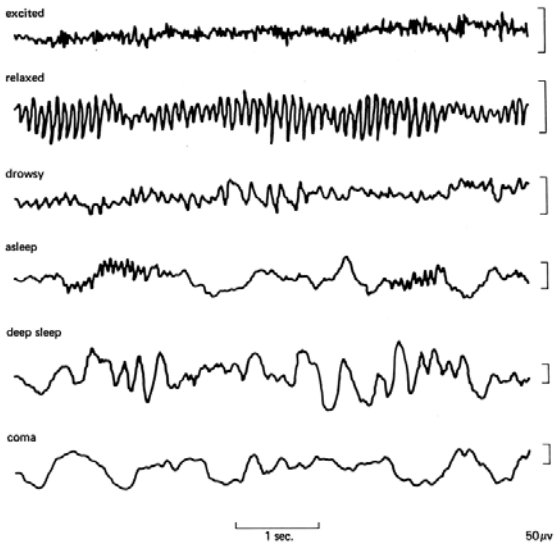

Figure 5: Neural activity (EEG's) and the corresponding behavioral states accompanying arousal levels including those associated with an awake excited person, the alpha rhythm associated with relaxation with eyes closed, the slowing in frequency associated with a drowsy condition, the slow high amplitude waves of sleep, the larger slow waves associated with deep sleep, and the further slowing of EEG waves associated with coma.

With decreasing states of consciousness, the EEG frequency slows and the amplitude increases. Additionally, with psychological milestones adapted from Piaget, one can notice a parallel growth

of brain weight and the average frequency of EEG background activity from posterior regions of the scalp as reflected in Figure 6.

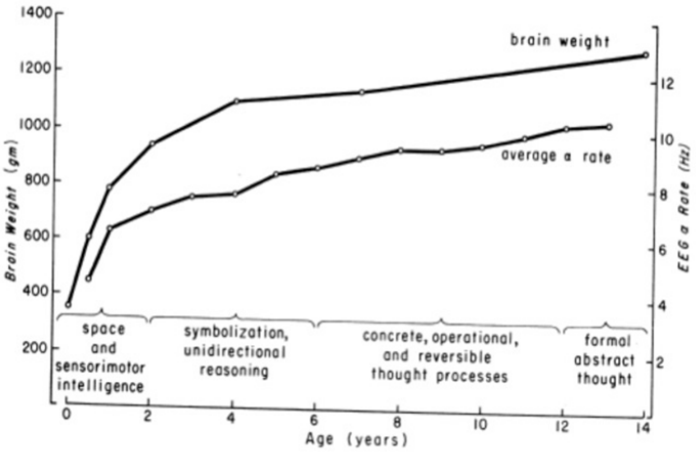

Figure 6: Parallel growth of brain weight and average frequency of EEG background activity from posterior regions of the scalp. Psychological maturation milestones adapted from Piaget [88,89].

Even though these measures of frequency by EEG are now considered relatively crude, they do provide a window into excitability within the brain. Researchers thought that problems arise when the operating speed of someone's brain is either too low (under-aroused) or too high (over-aroused). This is similar to the concept of hyperkinetic state or hypokinetic state. There is speculation that arousal levels may be the major component in a whole host of disorders. The goal of neurofeedback therefore is said to be to stabilize the brain and nervous system so that it does not fluctuate easily into over-arousal or under-arousal. Viewing the brain from this perspective returns us to some original theories of arousal that were popular in the 1950s. It was then thought that two main states existed, stability and arousal [90]. According to this theory, optimal idling speed for the human brain is about 14 Hz. Therefore, if the brain's major activities of speed lower than that 8-13 Hz, an individual may feel tired and might seek stimulation from coffee or stimulating behavior. Individuals might suffer from depression, ADD, and mild dissociative disorder. Alternatively, over-arousal might provoke an individual to feel unsettled and might then seek out alcohol to decrease arousal level or need medication to calm down, the situations being akin to depression versus mania or left versus right hemisphere dysfunction. Anxiety, hyper-vigilant stress, and obsessive behavior are thought to be all symptoms of over-arousal.

In the 1960s, neurofeedback was considered a revolutionary way to examine the mind and its capabilities. One of the early pioneers of biofeedback was M.B. Sterman, who was one of the first to experiment with a type of beta wave called sensory-motor rhythm (SMR) in the 12-15 Hz range. More specifically, a number of research studies confirmed the identification of a 12-14 Hz rhythm in the EEG of a number of species observed over the Rolandic (sensory-motor cortex). This rhythm is associated with inhibition of motor activity [91-93]. It was labeled sensory-motor

rhythm (SMR) for its location in the sensory motor cortex. The rhythm has also been identified in humans. An increase in SMR in the EEG of cats by operant conditioning was subsequently demonstrated [94].

Similar findings were found in primates. One effect of such training in cats and in humans was to increase the incidence and duration of Rolandic sleep spindles, which occur in the identical spectral band (12-15 Hz) as the waking SMR and in the same location. This is accompanied by more sustained periods of quiet sleep in both normal subjects and insomniacs [95]. It was also noted that paraplegics and quadriplegics exhibit larger than normal amounts of sleep spindles and reduced amounts of low frequency (4-7 Hz) EEG activity. In addition, patients with spinal cord injuries exhibit a relative dearth of epileptic behavior. Additionally, cats with cervical dorsal column transection exhibit a heightened threshold for druginduced seizures. In one case it was noted in an epileptic patient who experienced upper cervical cord compression, following the injury his seizure activity disappeared [96]. These findings suggest the fundamental relation between the incidence of SMR rhythm and of motor induced seizures. Reduction of activity in the 4-7 Hz frequency band has also been demonstrated in monkeys during sleep, after administration of four anticonvulsant drugs. This suggests that excessive low frequency amplitude is indicative of insufficient cortical control and is a concomitant of susceptibility to seizure onset.

Following this postulation, it was found in 1969 that after training for enhanced SMR rhythm in cats, threshold for seizure onset was increased for chemically induced seizures [97]. Following this, EEG feedback training in poorly controlled epileptics showed reports of seizure reduction. Sterman achieved an average 66 percent reduction in seizure incidence in four epileptics using SMR enhancement training in combination with inhibition of excessive slow activity in 6-9 Hz region. Wyler and associates [98] showed that enhancement of EEG activity above 14 Hz and suppression of activity below 10 Hz was effective in seizure reduction. Synchronization of the EEG worsened seizure incidents where a desynchronization of EEG improved it [98].

Lubar and Bahler [99] took Sterman's work even further and in a different direction. He had noticed that hyperactivity decreased in patients treated for epilepsy and based on this created the protocol now used for treatment of ADHD. This is not considered entirely unexpected since hyperactivity may also be regarded in terms of insufficient motor inhibition and since EEG observables are similar in general to interictal epileptiform activity consisting of a relative increase of low frequency activity and a relative dearth of intermediate frequency activity (SMR and beta activity). The first study of the EEG biofeedback effectiveness with hyperactivity in their absence of seizure history was reported by Lubar and Shouse [100]. A number of behaviors associated with the hyperactivity were monitored and significant changes were observed for 8 of 13 behavioral categories. The EEG training was shown to be more effective than the use of stimulant medication (Ritalin alone).

A study by Lubar and Lubar [101] extends the technique to attentional defects and learning

disabilities. The appropriateness of doing this is based on long standing observations that more than 60 percent of the cases of learning disabilities exhibit EEG abnormalities [102]. The experimental protocol was complimented with training in the 15-18 Hz region associated with EEG activation in general and with arousal and focus. Changes in EEG were documented with power spectral density measurements, which were compared with those of normal subjects. The EEG biofeedback was also accompanied by academic training. Acquisition of the desired EEG characteristics was observed in all six subjects under study. Significant improvement in academic performance was also documented for all of the subjects. It has been noted that ADD and ADHD have a strong neurological basis with increased beta activity occurring over central and frontal portions of the cortex and decreased beta activity occurring centrally, posteriorly, and sometimes even frontally. Beta activity has been associated with daydreaming and a lack of beta activity with poor ability to concentrate and to complete task.

Biofeedback treatment for ADD and learning disability typically involves approximately 50 sessions initially carried out 2-3 times a week and then phased out over a period. A session may consist of playing some kind of computer game in which a smiling Pacman gobbles up globs or a balloon that tries to float up to the sky while the patient's brain waves are continuously monitored. Each time the brain wave finds their way to the optimal state set by the clinician, the patient is rewarded with positive feedback. Pacman eats his enemy with pleasant tones. After anywhere from 5-50 sessions the brain seems to be able to find the optimal state on its own. Examining this information based on our previously described neurological model, we can see that consistent with these EEG studies, decreased activity or arousal of the brain, especially over somatosensory and frontal cortices, is associated with epilepsy, ADD, ADHD and learning disabilities. In addition, increasing activity to the somatosensory cortex has been shown to significantly improve these conditions. EEG activity is produced by the ascending activation system from the thalamus. Synchronization results from decreased thalamic activity and decreased desynchronization from increased thalamic activity. These studies also show that there is a relationship with activity from input from the dorsal column, its effect on EEG activity, and with the production of abnormal EEG activity.

In addition, the dorsal column projections to the cerebellum and thalamus and subsequently to the somatosensory cortex and frontal lobe seem to be the basis of gamma oscillations and overall brain baseline activity. Therefore, this would seem to confirm that decreased cerebellar and thalamic activation of the brain as a whole and the frontal lobe specifically is associated with decreased stability and function of the brain pathways and their processing capability. EEG may be an effective remediation tool because cognitive activation of frontal lobe will activate ascending pathways from the cerebellum and thalamus, as well as descending frontal projections to the brainstem reticular formation, basal ganglia, and will increase muscle tone with subsequent feedback through spine cerebellar and dorsal column pathways to cerebellar-thalamic and cortical projections. The benefit of EEG is that it is a relatively low level output, which will not

exceed the metabolic rate of neuronal pathways. However, neurofeedback therapists do not consider hemispheric differences and therapy does not appear to be specific to one hemisphere. In addition, if the problem arises from the musculoskeletal system and its lack of feedback as in a neck injury, this intervention strategy will not be effective in effecting change in the region of primary involvement. Whereas stimulating motor activity may be more specialized to a specific hemisphere and found to be more easily used in children, especially ones demonstrating hyperactive behavior and attentional deficits.

Sensory-Motor Intervention Strategies

Therapeutic use of light

Levitan and associates [103] reported that evidence exists from clinical, epidemiological, and neuroimaging studies that ADHD and seasonal affective disorder (SAD) have several features in common. They assessed SAD symptoms in adults with ADHD. One hundred and fifteen individuals attending an adult ADHD clinic in Toronto, Canada were asked to complete the Seasonal Pattern Assessment Questionnaire. The rate of SAD in the overall clinic sample was estimated at 19.1 percent, a prevalence rate significantly greater than rates reported in large population surveys at similar latitudes.

Decreasing or increasing the amount of light, varying the color of light, or blocking out light from certain fields of vision, have been used for many different conditions. These conditions include forms of depression, anxiety, learning disabilities, and sleep disorders, etc. One of the most recognized disorders that have been treated with the use of light is seasonal affective disorder or SAD. In a recent New York City survey, more than one third of responding adults reported at least mild winter malaise: 6 out of 100 reported severe depression [104]. It is thought that SAD, as well as other similar disorders are due to the affect that light has on regulating of biological or circadian clocks.

The first experiments of biological clocks date back to 1911 and were conducted by Karl Von Frisch, an Austrian zoologist. Von Frisch discovered that Minnows did not respond to ambient light perceived through their eyes. Von Frisch thought that something deep inside the brain itself could respond directly to light. He later traced this affect to the minnows' pineal gland, which we now know to be the source of melatonin. In the brain, a group of cells known as the supra-chiasmatic nucleus of the hypothalamus or SCN is thought to be the basis of biological clocks [105]. In mammals, it appears to be remarkably reliable. Even when removed from an experimental organism and placed in a dish, it continues to keep time on its own for approximately a day. The SCN is divided into two structures. One is the right hemisphere and one is in the left, just below and behind the eyes. Each part of the SCN is made up of approximately 10,000 densely packs neurons. Recent research in mice suggests that mammals have a set of special photoreceptors in their eyes, which react to light signals and carry them directly to the SCN. These photoreceptors are thought to be different from the rods and cones used to perceive light stimulating the retina. It

is thought that light helps to reset the biological clocks. Light in the morning is thought to set the clock ahead and in the evening, backwards. Whether the running of these biological clocks is an innate quality of cells or a product of some unseen force, like gravity, is not known. Nevertheless, disruption of light stimuli can disrupt these clocks.

Many other areas of the brain are affected by light. We can recall our earlier discussion of the intricacies of the development and function of the ventral and dorsal visual systems and their role in cognitive perception and limbic system function. We recall that the dorsal visual system is associated more with right hemisphere function, which is involved in global or low frequency stimulation. The ventral visual system is associated more with left hemisphere function, specific for a local visual function or higher frequency stimulation. These systems are powerfully connected to cognitive and emotional functions.

Modulating the frequency of the stimulus can change the firing rate of the thalamus and the brain as a whole. However, different frequencies of the same stimulus may have asymmetric affects on the brain. Modulating the frequency of stimulus also takes into account the metabolic rate of brain cells. Interestingly, it has been noted that red, which is a low frequency source, would be expected to slow down the neocortex and affect more of the right brain, increasing sympathetic responses. Blue light would be expected to speed up the firing rate of the neocortex, (thereby inhibiting sympathetic and exciting parasympathetic responses) which also may be more specific to left brain and in fact, has been shown to increase parasympathetic functions [106]. It has also been noted that a pale light blue paint on the walls of schools appears to decrease hyperactivity in children, where pale yellow on the walls of schools appears to improve concentration and learning abilities.

Altering the balance of light or vision from one hemisphere to the other has also been shown to have powerful psychological affects. Frederick Schiffer has found that using a pair of glasses that block vision to either the right or left hemispheres can help alleviate anxiety or depression [107,108]. Schiffer thinks that these glasses that work to relieve anxiety and distresses is remarkable testimony to the link between the eyes and the two sides of the brain and a variety of psychological problems. Schiffer attempted a simple experiment on himself. When he covered one eye and part of the other, he detected a slight difference in his clarity of thought. Schiffer then made safety glasses that covered one eye completely and half of the other. He had seventy patients suffering from severe anxiety wear the glasses and measured the affect on a one to ten scale, by which anxiety is calculated. Sixty percent of those patients had a 1-point difference (improvement on the scale) and 23 percent had a 2-point difference. Schiffer also had the patients wear glasses that covered the other eye. In interviews, 40 of the patients said they felt more anxiety when they wore the glasses. A study of a control group of college students, who were not in therapy, also found measurable changes in their feelings of anxiety and changes in brain wave patterns with the glasses. Although no significant knowledge base at present exists in the application of light to

the remediation of neurobehavioral disorders of childhood, the existing theory supports it further investigation.

Various forms of visual imagery have been found to help improve intelligence, motor performance, and behavior. Guided imagery is one form of visualization. Guided imagery has the subject create internal scenarios and mental pictures that evoke positive physical responses. Imagery is reported to improve the immune system [109] and reduce stress [110].

Leiner and associates [111] have noted that several studies of ideation or mental imaging show significant blood flow changes to the cerebellum and frontal lobe. If individuals imagine a motor act like playing tennis or a cognitive act like mental calculation, both show significant increases in different areas of the cerebellum and neocortex. On the other hand, it has been shown that those who imagine shooting a basketball display as much improvement in that skill after a week as those who actually physically practice shooting a basketball. This would lead us to think that whether imagined or actually done, motor acts must activate similar area of the cerebellum that create functional improvement in motor control.

In the last decade, there has been a dramatic increase in research effectively integrating cognitive psychology, functional neuroimaging, and behavioral neurology. This new work is typically conducting basic research into aspects of the human mind and brain. Parsons [112], in one study the authors employed object recognition, mental motor imagery, and mental rotation paradigms, to clarify the nature of a cognitive process, imagined spatial transformations used in shape recognition. Among other implications of the study was that recognizing a hand's handedness or imagining one's body movement depends on cerebrally lateralized sensory-motor structures and deciding upon handedness depends on exact match shape confirmation. In a second study, using cutaneous, tactile, and auditory pitch discrimination paradigms, it was suggested that the cerebellum has non-motor sensory support functions upon which optimally fine sensory discriminations depend. Mental imagery, the generation and manipulation of mental representations in the absence of sensory stimulation, is a core element of numerous cognitive processes. Numerous investigators have recently investigated the cortical mechanisms underlying imagery and spatial analysis in the visual domain using event-related functional magnetic resonance imaging during the mental clock task [113] and fMRI [114]. The timeresolved analysis of cortical activation from auditory perception to motor response reveals a sequential activation of the left and right posterior parietal cortex, suggesting that these regions perform distinct functions in imagery tasks.

Knauff and colleagues found that in the absence of any correlated visual input, reasoning activates an occipital-parietal-frontal network, including parts of the prefrontal cortex (Brodmann's area, BA, 6, 9) and the cingulate gyrus (BA 32), the superior and inferior parietal cortex (BA 7, 40), the precuneus (BA 7), and the visual association cortex (BA 19). Because reasoners envisage and inspect spatially organized mental models to solve deductive inference problems, we do have a basis for concluded that imagery has the capacity for effecting change in brain state. In one of

the view imaging studies to date on clinical applications of imagery as a therapeutic tool, Marks and associates [115] investigated subjective imagery in obsessive-compulsive disorder before and after exposure therapy using fMRI. A small randomized study was performed, with controls for type and order of mental imagery and for treatment condition (exposure therapy guided by a computer or by a therapist, or relaxation guided by audio-tape). Before and after treatment, during fMRI scanning, patients imagined previously rehearsed scenarios that evoked an urge to ritualize, non-OCD anxiety, or a neutral state, and rated their discomfort during imagery. The method evoked greater discomfort during OCD imagery and anxiety (non-OCD) imagery than during neutral imagery. Discomfort was reduced by canceling imagery. Discomfort during OCD imagery (but not during anxiety non- OCD imagery) fell after exposure therapy but not after relaxation. The results showed differences between OCD and non-OCD images and their change after successful treatment, and confirmed clinical suggestions that canceling images reduced OCD discomfort.

Therapeutic use of sound

Music has a unique capacity to reorganize cerebral function where it has been damaged [7,116]. "There's an overlap in brain mechanisms in the neurons used to process music, language, mathematics and abstract reasoning," Mark Tramo, a neuroscientist at Harvard Medical School has stated, [117]. "We think a hand full of neuronal codes is used by the brain, so exercising the brain through music strengthens other cognitive skills. It's a lot like saying if you exercise your body by running, you enhance your ability not only to run but also to play soccer or basketball."

Various techniques use sound and music as their primary mode of therapy. These techniques have reportedly been affective for children with learning disabilities and behavioral problems. There are those who think that sound and music can effects dysfunction in the nervous system through both its calming and energizing affects on the brain and CNS. As a clinical therapy it is used in hospitals, schools and psychological treatment programs to reduce stress or lower blood pressure, alleviate pain, overcome various learning disabilities, improve movement and balance, and promote endurance and strength.

Campbell, author of the book The Mozart Effect, has researched the affect of music and its therapeutic affect [118]. He thinks that since development of the first musical instruments between 43,000 – 82,000 years ago, humans knew that music created special effects. He suggests that music in the form of song and dance preceded speech in humans and was the first form of language. He states that research has shown that two-thirds of the inner ear cilia (hair cells) resonate only at the higher music frequency's 13,000 – 20,000 hertz. To indicate that the application of the so-called Mozart Effect is without controversy would be an understatement especially considering there have been numerous reports of an inability to replicate the effect [119].

Hughes and Fino [120] had performed a study reported in Clinical Electroencephalography The goal of this study was to determine distinctive aspects of Mozart music that may explain the

Mozart Effect, specifically, the decrease in seizure activity. As many as 81 musical selections of Mozart, but also 67 of J.C. Bach, 67 of J.S. Bach, 39 of Chopin and 148 from 55 other composers were computer analyzed to quantify the music in search of any distinctive aspect and later to determine the degree to which a dominant periodicity could be found. Long-term periodicity (especially 10-60 sec, mean and median of 30 sec), was found often in Mozart music but also that of the two Bachs, significantly more often than the other composers and was especially absent in the control music that had no effect on epileptic activity in previous studies. Short-term periodicities were not significantly different between Mozart and the Bachs vs. the other composers. The conclusion is that one distinctive aspect of Mozart music is long-term periodicity that may well resonate within the cerebral cortex and also may be related to coding within the brain.

Thompson and Andrews [121] in reporting on the Mozart effect in which they claim was made that people perform better on tests of spatial abilities after listening to music composed by Mozart, examined whether the Mozart Effect is a consequence of between-condition differences in arousal and mood. Participants completed a test of spatial abilities after listening to music or sitting in silence. The music was a Mozart sonata (a pleasant and energetic piece) for some participants and an Albinoni adagio (a slow, sad piece) for others. These investigators also measured enjoyment, arousal, and mood. Performance on the spatial task was better following the music than the silence condition but only for participants who heard Mozart. The two music selections also induced differential responding on the enjoyment, arousal, and mood measures. Moreover, when such differences were held constant by statistical means, the Mozart Effect disappeared. Thompson's findings provide compelling evidence that the Mozart Effect is an artifact of arousal and mood. We are here less concerned about Mozart as a composer and more about the effects of sound in effecting change in brain and cognitive function.

Thompson and Andrews [121] in their paper provide an overview of the theoretical underpinnings of the Tomatis Method, along with a commentary on other forms of sound/music training and the need for research. A public debate was sparked over the Mozart Effect. This debate has turned out to be unfortunate because the real story is being missed. The real story starts with Alfred Tomatis. Dr. Tomatis was the first to develop a technique using modified music to stimulate the rich interconnections between the ear and the nervous system to integrate aspects of human development and behavior. The originating theories behind the Tomatis Method are reviewed by Thomson and Andrews to describe the ear's clear connection to the brain and the nervous system. The neuropsychology of sound training describes how and what the Tomatis Method affects. The 50 years of clinical experience and anecdotal evidence amassed by Tomatis, shows that sound stimulation can provide a valuable remediation and developmental training tool for individuals with neurobehavioral disorders.

In Norway, in the 1980's, educators used music therapy for children with severe physical and mental disabilities. They found that music reduced muscle contraction in patients' with severe spastic conditions, increased range of motion in their spines, arms, hips, and legs. These effects

would suggest effects not only on the neocortex, but the brainstem reticular formation as well as the cerebellum. Since music has powerful effects on the hair cells in the vestibular apparatus, it would also be expected to have effects on the olivary complex and the cerebellum. This, in fact, may be its primary effect.

A common intervention that has been employed with children with ADD, learning disabilities, and central auditory processing, or CAP deficits involves attempts to influence activity in the cerebellar-vestibular system (CVS) by auditory stimulation in frequency ranges generating hyperacusis and discomfort. Ann Blood and colleagues [122,123], conducted the first scientific studies on music's emotional impact on the brain. They employed positron emission tomography PET to examine cerebral blood flow (CBF) changes related to affective responses to music. Ten volunteers were scanned while listening to six versions of a novel musical passage varying systematically in degree of dissonance. Reciprocal CBF covariations were observed in several distinct paralimbic and neocortical regions as a function of dissonance and of perceived pleasantness/unpleasantness. The findings suggest that music may recruit neural mechanisms similar to those previously associated with pleasant/unpleasant emotional states, but different from those underlying other components of music perception, and other emotions such as fear. In a subsequent study, Blood's group again employed PET to study neural mechanisms underlying intensely pleasant emotional responses to music. Cerebral blood flow changes were measured in response to subject-selected music that elicited the highly pleasurable experience of "shivers-down-the-spine" or "chills." Subjective reports of chills were accompanied by changes in heart rate, electromyogram, and respiration. As intensity of these chills increased, cerebral blood flow increases and decreases were observed in brain regions thought to be involved in reward/motivation, emotion, and arousal, including ventral striatum, midbrain, amygdala, orbitofrontal cortex, and ventral medial prefrontal cortex. These brain structures are known to be active in response to other euphoria-inducing stimuli, such as food, sex, and drugs of abuse. This finding links music with biologically relevant, survival-related stimuli via their common recruitment of brain circuitry involved in pleasure and reward.

Others (112,124,125] have observed significant increase in the function of the cerebellum in studies that examine the neuroanatomy of expert musicians as they listen to music. It has been known for sometime that children develop an early appreciation for music. In the first year of life, children have been shown to pay attention more acutely to stimuli with a harmonic structure, and it seems that they learn music in the same way as language, with one note exponentially acquiring new ones [126]. In the past few years, researchers have begun to map areas of the brain involved in performing music or while silently reading scores. However, no previous studies have examined the emotions elicited during a musical piece. A more complete review can be found in [116].

Blood and her colleagues, decided to target the emotional response to music, by studying ten adults from ages 19-43, as they listened to musical notes that either clashed or had a harmonic

tone. They designed the experiment using a single melody and adding on six versions from a very pleasant sounding piece to something that a two-year-old would bang out on the piano. They measured blood flow in the brain during these experiences to see if they would find a difference. According to Blood, the discordant notes triggered activity in the parahippocampal gyrus, an area near the temporal lobe that plays an important role in processing sensory memory. When the music was pleasing to the subjects, the investigators found significant activity in the lower region of the frontal lobe. Responses were primarily found on the right side of the brain. Blood and colleagues think this activation as an indication of the emotional responses to music. These brain regions were also different from the region activated when musicians read a score, or were asked to pick out mistakes in musical pieces. In 1992, researchers at the Montreal Neurological Institute published the first study using PET to identify areas of the brain active during musical tasks. The late Justine Sergent and her colleagues studied musicians as they read scores or performed, and found many areas of the brain were involved in converting the written score into finger movement.

Lawrence Parsons and his colleagues [112], advancing Sergent's studies, found that specific tasks called upon during the musical experience rely on different areas of the brain. In one study, subjects were eight right-handed faculty conductors. The conductors were instructed to focus on errors in melody, harmony, or rhythm in a Bach Choral. The errors appeared one to every two beats and the musicians were instructed to take notice but not to perform any motor responses. Each task was shown to produce very different patterns of brain activity. Melody activated both the left and right hemispheres in the temporal lobe, while harmony and rhythm triggered activity more in the left hemisphere. Harmony did not activate the temporal lobe at all. Each of the tasks also activated right fusiform gyrus. This same area in the left hemisphere has been linked to visual processing of words. Researchers suspect that the right fusiform gyrus may have evolved to regulate information on musical notes and passages. It has been noted that stroke patients who have lost language function may be able to gain some verbal improvement, by singing words, which Parsons' thinks may be facilitated by this region of the brain. Listening for errors in harmony, melody, and rhythm also activate the cerebellum even though the conductors were not moving, indicating the cerebellum's involvement in cognition.

Schlaug [125] reported that skilled male musicians he studied have larger cerebella than average. He employed CT scans to compare 32 right-handed male musicians with 24 right-handed men with no musical training. Schlaug and his colleagues [127] have previously reported that male musicians have larger corpus callosa and larger primary motor cortices in the frontal lobe. They have not found similar differences in the cerebellar volumes between male musicians and nonmusicians. Other studies have shown functional brain changes in individuals who have mastered certain skills or suffered brain damage; this is the fist study that has identified structural changes in the brain that are associated with a learned skill. This indicates that the cerebellum is involved in both motor and cognitive function and in the processing and the production of music.

An interesting parallel exists between brain changes associated with the acquisition of a

musical skill [125] and languages acquisition [111]. Leiner and associates have noted that the lateral areas of the cerebellum are activated during the cognitive aspects of speech production, whereas, the medial cerebellar cortex is activated during the motor function of speech. If music were indeed the first form of human language, then we would expect to find a parallel between music and language processing in the cerebellum, thalamus, and frontal lobe. It is also interesting to note that musicians have been found to demonstrate structural changes in the cerebellum, frontal lobe (motor cortex), and the corpus callosum. Since the cerebellum is thought to act as an association cortex external to the neocortex, especially between the dorsal and ventral language areas, it may assist in integrating function of the hemispheres. This being the case, we may expect to see an enlargement in the corpus callosum associated with hemispheric integration. Since both the corpus callosum and the cerebellum may be involved in the temporal synchronization of multiple areas, this may be the reason for the observed enlargement.

This may also explain the results of a study by Chan and her colleagues [128] and others [116,129], that indicate that children who spend a few years learning to play a musical instrument, also develop better verbal skills compared with those who never studied music. These findings seem to be consistent with the brain scans that have shown the left planum temporale to be larger in musicians than in individuals without extensive training in instrumental music. Chan and associates [128] studied 60 female college students from the University of Hong Kong, of whom 30 had at least 6 years of training with western musical instruments before the age of twelve and the other 30 had no formal training. The students were tested for verbal memory by attempts to remember lists of words. The researchers stated, "We found that adults with music training learn significantly more words than those without any music training." However, they found adults with and without music training was not significantly different in their ability to remember visual images such as words written on paper.

According to Evan Balaban, "There has been a long tradition of researchers trying to segregate speech and muscle in the brain. There is now evidence from several studies that they (music and speech), may have more to do with each other than was previously thought." If musically trained individuals had structural changes (the planum) as well as functional language changes that non-musicians do not have, the main differences in ability between them would be the motor acts associated with playing music and possibly the breathing associated with wind instruments [130,131]. Both of these differences in ability and the functional changes associated with them can be attributed to the effects of the cerebellum. This would also demonstrate that motor activities have a carry-over effect on cognitive function of the frontal lobe, such as in the case of verbal memory.

Musically trained brains respond to randomly heard musical tones in fundamentally different ways than those who are untrained. This effect is apparently more pronounced among those who take music lessons before the age of six. Recent studies suggest [125,132-134] that when a piano tone is played, either more neurons are activated or the neurons are responding in a more

synchronized fashion. No change occurs in those without musical training. In one study, German researchers asked 20 musicians from a local conservatory were asked to watch a cartoon, while either pure non-musical tones or piano tunes were presented. They measured electrical activity in the brain during the activity. A control group of non-musicians heard the same tones. The results of this study conducted by Christo Pantev and colleagues found that musically trained brains showed about 25 percent more activity than non-musicians. What was also interesting is that the effect was observed only when piano tones were presented to musicians. Pure tones, which are not musical, had no apparent effect. In addition, those who began lessons before their sixth birthday seemed to have the strongest response. It was also noted that the brains of musicians respond differently to piano tones [133].

Penhune, Zattore, and Evans [135] reported that there exists a difference in brain activities measured by PET scans in musicians with perfect pitch (the ability to hear a tone and name it) compared to those with relative pitch (the ability to recognize the difference between a major and a minor note). The recorded activity differences were noted in the left frontal cortex in those with perfect pitch. When those with relative pitch were asked to choose between a major and minor note, this region in the frontal lobe also became active. The authors concluded that those with perfect pitch were processing the information more efficiently. The left frontal lobe is the motor speech area connected with activation of the right cerebellum. With this recent increase in research showing the effects of music on the brain, music as therapy has gained wider acceptance in more mainstream centers.

Therapeutic use of olfaction

The sense of smell can be used as a powerful stimulus to the brain. A number of recent investigations have suggested a significant role for olfactory stimulation in the alteration of cognition, mood, and social behavior. These orthodox investigations have a common, if uneasy, relationship with the holistic practice of so-called aromatherapy. In children and adults, various studies have shown improvement in learning abilities and emotional disturbances, as well as affects on blood pressure and stress responses. One study using peppermint oil has shown improvement in cognitive function on children as compared to controls [136]. In their study Soussignan and associates examined the facial responsiveness of ten mutic children with pervasive developmental disorder (PDD) and ten normal children matched for sex and chronological age who were all covertly videotaped while presented with a set of odors contrasted in hedonic valence. Hedonic ratings of the stimuli were obtained from both the group of normal subjects and a panel of adults. Two methods were used to measure facial responses in the same subjects. The first method consisted in an analysis of facial movements with the Facial Action Coding System. Results show that PDD and normal subjects displayed distinct action units in response to unpleasant odors. PDD subjects typically displayed muscular actions indexing negative experience, while normal subjects showed more smiles. With the second method, a panel of observers rated odor-elicited facial behavior. The observers were asked to judge whether the subjects were exposed a

pleasant, neutral, or unpleasant smell. The facial responses to unpleasant odors were classified more accurately in PDD than in normal subjects. These findings suggest a functional ability to sense the hedonics attached to odors, but a deficit of socialization of hedonic facial displays in developmentally disordered subjects.

Murphy, Barkley and Bush [137] examined 105 young adults with attention deficit-hyperactivity disorder (ADHD) who were compared with a control group of 64 normals on 14 measures of executive function and olfactory identification. The ADHD group performed significantly worse on 11 measures with no Group X Sex interaction, contrary to the findings of Ceccarelli and colleagues [138] in rats. No differences were found in the ADHD group as a function of ADHD subtype or comorbid oppositional defiant disorder. After IQ was controlled, some group differences in verbal working memory, attention, and odor identification were no longer significant, whereas those in inhibition, interference control, nonverbal working memory, and other facets of attention remained so. The deficits in olfactory identification see in neurobehavioral disorders in part can serve as a basis for therapeutic intervention in this modality as well as others.

Further support for the use of olfactory stimulation as part of an overall intervention strategy in neurobehavioral disorders of childhood comes from the study of Levy and colleagues [139] who noted that memory for odors induces brain activation as measured by functional MRI. fMRI brain scans were obtained in 21 normal male and female subjects and in in two patients with hyposmia or diminished sense of smell in response to the imagination of odors of banana and peppermint and to the actual smells of the corresponding odors of amyl acetate and menthone, respectively. In normal subjects, brain activation in response to imagination of odors was significantly less than that in response to the actual smell of these odors, and activation following imagination of banana odor was significantly greater in men than in women, for the actual smell of the odor of amyl acetate. The ratio of brain activation by imagination of banana to activation by actual amyl acetate odor was about twice as high in women as in men. Before treatment, in patients with hyposmia, brain activation in response to odor imagination was greater than after presentation of the actual odor itself. After treatment, in patients with hyposmia in whom smell acuity returned to or toward normal, brain activation in response to odor imagination was not significantly different quantitatively from that before treatment; however, brain activation in response to the actual odor was significantly greater than that in response to imagination of the corresponding odor. Brain regions activated by both odor imagination and actual corresponding odor were similar and consistent with regions known to respond to odors. Their study indicates that (a) odors can be imagined and similar brain regions are activated by both imagined and corresponding actual odors; (b) imagination of odors elicits quantitatively less brain activation than do actual smells of corresponding odors in normal subjects; (c) absolute brain activation in men by odor imagination is greater than in women for some odors, but on a relative basis, the ratio for odor imagination to actual smell in women is twice that in men; (d) odor imagination, once the odor has been

experienced, is present, recallable, and capable of inducing a relatively constant degree of brain activation even in the absence of the ability to recognize an actual corresponding odor.

Henkin and Levy [141] looked further at the nature of the lateralization of brain activation to imagination and smell of odors also using fMRI finding a left hemispheric localization of pleasant and right hemispheric localization of unpleasant odors. fMRI brain scans were obtained in 24 normal subjects in response to imagination of banana and peppermint odors and in response to smell of corresponding odors of amyl acetate and menthone, respectively, and of pyridine. The results indicated that in normal subjects, activation generally occurs in the direction of left (L) to right (R) brain hemisphere in response to banana and peppermint odor imagination and to smell of corresponding odors of amyl acetate and menthone. There are no overall hemispheric differences for pyridine odor. Localization of all lateralized responses indicates that anterior frontal and temporal cortices are brain regions most involved with imagination and smell of odors. Imagination and smell of odors perceived as pleasant generally activate the dominant or L to R brain hemisphere. Smell of odors perceived as unpleasant generally activates the contralateral or R to L brain hemisphere. According to these authors, predominant L to R hemispheric differences in brain activation in normal subjects occur in the order amyl acetate > menthone > pyridine, consistent with the hypothesis that pleasant odors are more appreciated in left hemisphere and unpleasant odors more in right hemisphere. Anterior frontal and temporal cortex regions previously found activated by imagination and smell of odors accounted for most hemispheric differences.

Henkin and Levy [141], in a more recent study again employed fMRI to define brain activation in response to odors and imagination ("memory") of odors and tastes in patients who never recognized odors (congenital hyposmia). These authors studied nine patients with congenital hyposmia as they responded to odors of amyl acetate, menthone, and pyridine, to imagination ("memory") of banana and peppermint odors, and to salt and sweet tastes. Functional MR brain scans were compared with those in normal subjects and patients with acquired hyposmia. The authors found that brain activation in response to odors was present in patients with congenital hyposmia, but activation was significantly lower than in normal subjects and in patients with acquired hyposmia Regional activation localization was in anterior frontal and temporal cortex similar to that in normal subjects and patients with acquired hyposmia. Activation in response to presented odors was diverse, with a larger group exhibiting little or no activation with localization only in anterior frontal and temporal cortex and a smaller group exhibiting greater activation with localization extending to more complex olfactory integration sites. "Memory" of odors and tastes elicited activation in the same central nervous system regions in which activation in response to presented odors occurred, but responses were significantly lower than in normal subjects and patients with acquired hyposmia and did not lateralize. Odors induced CNS activation in patients with congenital hyposmia, which distinguishes olfaction from vision and audition since neither light nor acoustic stimuli induce CNS activation.

Henkin and Levy concluded that odor activation localized to anterior frontal and temporal cortex is consistent with the hypothesis that olfactory pathways are hard-wired into the CNS and that further pathways are undeveloped with primary olfactory system CNS connections but lack of secondary connections. However, some patients exhibited greater odor activation with response localization extending to cingulate and opercular cortex, indicating some olfactory signals impinge on and maintain secondary connections consistent with similar functions in vision and audition. Activation localization of taste "memory" to anterior frontal and temporal cortex is consistent with CNS plasticity and cross-modal CNS reorganization as described for vision and audition. Thus, there are differences and similarities between olfaction, vision, and audition; the differences are dependent on the unique qualities of olfaction, perhaps due to its diffuse, primitive, fundamental role in survival. These studies add further support in employing odor intervention strategies in neurobehaviorally-involved children in programs of differential hemispheric activation.

The effect of the olfactory system on the limbic system is profound especially when we consider the evolutionary development of the brain. The limbic system is intimately connected to the rhinencephalon or primitive "nose brain." Therefore, we would expect that odors or pheremonal activity would have direct affect on emotions, autonomic regulations, and through effects on the parahippocampal complex, on memory acquisition. Although it has been generally accepted that the sense of smell is the only sense that is not related to the thalamus, there has been recent evidence of a hypothalamic-thalamo-cortical circuit mediates pheremonal influences on eye and head movement [142]. Through this mechanism, pheremonal activity is thought to regulate attentional mechanisms. Risold and Swanson used a method for simultaneous iontophoretic (movement of ions as a result of an applied electric filed) injections of anterograde tracer phaseolus vulgaris leukoagglutinin and the retrograde trace of flora gold was used to characterize in the rat a hypothalamicthalamo- cortical pathway ending in a region thought to regulate attentional mechanisms by way of eye and head movement.

The investigators thought that the relevant medial hypothalamic nuclei receive pheremonal information from the amygdala and project to specific parts of the thalamic nucleus reuniens and antero-medial nucleus, which then projects to a specific lateral part of the retrosplenial area (or medial visual cortex). They note that this area receives convergent input from the lateral posterior thalamic nucleus and projects to the superior colliculus. In addition, bi-directional connections with the hippocampal formation suggest that activity in this circuit is modified by previous experience. They further note that there are striking parallels with basal ganglia circuitry. In discussion of their results, they note that their evidence suggests that the rostral medial zone nuclei of the hypothalamus participate in a thalamo-limbic projection similar to the classic mammillo-thalamic limbic projections from the caudal medial zone and that the former receives olfactory information and modulates well established attention mechanisms involving eye and head movement.

In regard to intra-cortical projections of the retro-splenial area, these are divided into three streams. One major stream extends rostrally to end in the anterior cingulate caudal pre-limbic and ventral lateral orbital areas. They note that their double injection results suggest that the first two areas project back to the retrosplenial area. This is of interest because in the rat, anterior and to a lesser extent caudal pre-limbic areas are thought to be associated with the frontal eye fields along with the adjacent secondary motor areas mainly because they project to several brainstem regions involved in ocular motor control including the superior colliculus [143]. It is also noted that the anterior cingulate and the secondary motor areas receive inputs from the lateral posterior thalamic nuclei [142] and the medial dorsal nucleus No. 17 [144]. The anterior cingulate area receives input from the lateral dorsal nucleus No. 20 [145] and the rostral nucleus reuniens.

Risold and Swanson [142] suggest that information arriving at the rostral medial hypothalamus from pheremonal cortex (in the cortical medial amygdala) projects to the mid-brain motor regions by descending pathways, as well as to parts of the cerebral cortex involved in regulating eye and head movements by ascending pathways to the rostral nucleus reuniens and ventral intermedial nucleus. They note that the hippocampal formation participates in conceptually similar circuitry involving the caudal medial hypothalamus (mammillary body), which is thought to give rise to the mammillo-thalamic and mammillo-tegmental tracks. Iso-cortical regions project to the basal ganglia, which in turn generate descending projections to mid-brain motor regions and ascending projections to secondary motor cortical regions by way of the ventral anterior thalamic nucleus.

In summary Risold and Swanson [142] state that their model predicts that the rostral nucleus reunions and ventral anterior medial nucleus projecting to the retrosplenial area pathway, conducts pheremonal information to a polymodal cortical mid-brain pathway eliciting attentional motor responses involved in the procurement phase of appropriate motivated or goal directed behavior. We know that goal directed behavior is a function of the prefrontal cortex and approach and avoidance behavior. Olfactory stimulation therefore would be expected to increase frontal cortex activation through its affect on orbital-frontal and frontal eye fields, as well as secondary motor cortex. Olfactory stimulation affects limbic structures like the amygdala and hypothalamus, which regulate emotional and autonomic responses and which are inhibited by frontal cortical activity. It can also influence learning and memory through its affect on the hippocampal formation and intra-hippocampal circuit. The intra-hippocampal circuit plays a critical role in short-term episodic or declarative memory [142].

Olfactory stimulation also affects the anterior and posterior cingulate areas, which have been implicated in several aspects of spatial memory [146]. By affecting attentional mechanisms of eye and head movements, it would also be expected that there may be influence on cerebellar activity either through affects on ocular-motor or brainstem motor nuclei. Therefore, the use of olfactory therapy or pheremonal activity has a neurophysiological basis for affecting both learning abilities and behavioral and emotional disorders.

Integrated Sensory-Motor Intervention Strategies

According to practitioners, Occupational Therapy is a health profession concerned with improving a person's occupational performance. In a pediatric setting, the Occupational Therapist deals with children whose occupations are usually players, preschoolers, or students. The Occupational Therapist evaluates a child's performance in relation to what is developmentally expected for that age group. If there is a discrepancy between developmental expectations and functional ability, the OT looks a variety of perceptual and neuromuscular factors, which influence function.

Jean Ayres is credited with having first identified sensory integrative dysfunction, which is defined as an irregularity or disorder in brain function that makes it difficult to integrate sensory input effectively. It is thought that sensory integrated dysfunction may be present in motor, learning, social, emotional, speech, language, or attention disorders. Ayres thought that proprioceptive input is extremely important to the function of the sensory system and the brain as a whole. She identified gravity as an important input to the central nervous system because of its constancy of input. She thought that the primary source of this proprioceptive and gravitational input was from the vestibular apparatus of the inner ear and the vestibular system. She called this the cerebellar vestibular system. She thought that this system was a primary force in brain development. This was insightful considering the paucity of research to then support her theories of the development and function of the brain. Her observations and results were impressive enough that now Occupational Therapy with its developmental early intervention focus is universally adopted.

The vestibular apparatus and its receptors do not vary their sensitivity or influence the brain directly. The balance and sensitivity of the apparatus is set by the function of the cerebellum and the function of the cerebellum is a product of the service of four major pathways: (1) the visual system, (2) the proprioceptive system from muscles and joints, especially the cervical spine, (3) the vestibular system, and (4) the cerebral cortex. Since the cerebral cortex is just forming in a developing child and the vestibular and visual systems are relatively constant, the proprioceptive system is by far the most important to the cerebellum and its effects on the thalamus and the neocortex.

Ayres observed that children with learning and neurobehavioral problems exhibit what she termed sensory defensiveness. It was thought that this sensory defensiveness was the result of an over-activation of our protective senses. It was noticed that some children had decreased responses to sensory stimuli and some appeared to have increased sensitivity to sensory input. We now have a better way of understanding and explaining these observations and realize that both are the product of decreased sensory input to the cerebellum, thalamus, and neocortex. The cerebellum has two halves as does the cerebrum. These two halves must be balanced in their activation. If they are not, the hemisphere with decreased activity may initially be less sensitive to

incoming sensory stimuli with an increased threshold of activation because the neurons are less active. However, over time, this decreased activation causes the cells to shift closer to threshold as a compensatory mechanism. This makes the child more sensitive to stimuli that affect the dysfunctional half of the cerebellum. Tactile, proprioceptive, extra-ocular, and vestibular input indeed results in over-firing of the cerebellum. The child will experience lower threshold to touch, movement of the head, neck, or body expressed as motion sickness, disordered eye movements, or visual perceptual disturbances. Cerebral activity associated with cognition or emotion also can make the cerebellum fire aberrantly and the cells, which have less endurance or fatigability to this input, may cause these cells to produce free radicals and result in oxidative stress injury to these same cells. In the basal ganglia this may produce hyperkinetic and/or hypokinetic behavior through the same process. In the cerebrum, we recognize this as epilepsy, epileptiform activity, or spontaneous firing of neurons [5,11,147].

Ayres observed the symptoms of this process and described several types of sensory defensiveness.

1. Tactile defensiveness: Children with tactile defensiveness avoid letting others touch them and would rather touch others. They frequently fuss or resist hair washing or cutting. They may act as if their life is being threatened when being bathed or having clothes changed. Some types of clothes, clothing labels, or new clothes often irritate these children. They may dislike being close to others or avoid crowds. People accidentally bumping into them can agitate them. They often do not like to get their hands or feet dirty. They may seem unnecessarily rough to people. Some may bump or crash into things on purpose as a way of seeking sensation or seen under responsiveness to certain sensations or pain.

2. Oral defensiveness: Some children dislike or avoid certain textures or types of foods. They may be over or under sensitive to spicy or hot foods, avoid putting objects in their mouth and/or intensely dislike teeth brushing or face washing. Sometimes have a variety of feeding problems since infancy.

3. Gravitational insecurity: This appears to be an irrational fear of change in position or movement. These children are often fearful of having their feet leave the ground or having their head tip backwards.

4. Postural insecurity: This is a fear and avoidance of certain movement activities due to poor postural mechanisms.

5. Visual defensiveness: This may involve an over sensitivity to light and visual distractibility. With this problem, children may avoid going outside in certain light and/or need to wear hats or sunglasses to block out light. They may startle more easily and/or overt their eyes or seem to avoid eye contact.

6. Auditory defensiveness: This reflects an over sensitivity to certain sounds and may involve

irritable or fearful responses to noises like vacuum cleaners, motors, fire alarms, etc. Children sometimes make excessive amounts of noise to block out sounds [148]. Other symptoms can include unusual sensitivity to taste and/or smell (cf. preceding section).

When we understand how the cerebellum functions and how it affects the thalamus and cerebral cortex, we will then be able to explain more fully all of the symptoms of autistic spectrum disorders as a primary deficit or imbalance of cerebellar-cortical activation. We remember that the primary output of the cerebellar cortical cells or Purkinje cells is inhibitory to the cerebellar output nuclei. The cerebellum also controls motor coordination, balance, postural stability, and extraocular eye movements. It also activates the thalamus, which relays all sensory input to the cerebrum. Decreased activation of the cerebellum results in its dysfunction even though it may be more sensitive to input and may cause decreased stability of thalamus and cerebrum, even though the overall level of stimulation is decreased. This decreased threshold or increased signal-to-noise ratio may cause the cells to fire prematurely, they may reach oxidative stress earlier. This increased sensitivity is a product of decreased activation and is perceived as unpleasant by the child. This explains why a child with the same problem can present differently with one being over-reactive to certain stimuli and another being under-reactive. The underlying problem is the same, a lack of the central nervous system being properly activated. The same lack of stimulation can produce hyperkinetic behavior, while another may present with hypokinetic behavior.

Ayres devised a number of ways of treating these problems of sensory defensiveness. In Occupational Therapy, the approach to treatment primarily involves vestibular, proprioceptive, and tactile stimulation along with behavior modification techniques. Examples of some of these treatments for particular problems are:

1. Tactile defensiveness: OT treatment approaches include applying rapid and firm pressure touch to arms, hands, back, legs, and feet with a non-scratching brush with many bristles. The brushes recommended are specific plastic surgical scrub brushes. This is followed by gentle joint compression to the shoulders, elbows, wrists, hips, knees, ankles and sometimes fingers and feet. This treatment is recommended because the results are effective for short periods. Occupational Therapists note that if these procedures are applied consistently over time, the defensiveness is permanently reduced or even eliminated. Deep pressure touch, compression, or traction to the joints and heavy muscle action together is a special combination to reduce or eliminate sensory defensiveness. (Summation of sensation that is neurologically experienced in a short period over a large body space).

2. Oral defensiveness: OT treatment of applying heavy pressure across the roof of the mouth and giving input to the temporo-mandibular joint. Oral motor activities are also used that involve biting or resistive sucking use with a knot on the end, fruit roll-ups, beef jerky, etc. to bite and pull on. Occupational Therapists use small straws, sports bottles, plastic tubes, etc. for sucking as well as mouth toys that involve sucking and blowing.

3. Gravitational and postural insecurity: In which treatment includes jumping on bouncing surfaces, trampolines, bed mattresses, or on the floor with jarring action, jumping and crashing into piles of pillows or beanbag chairs, bouncing while sitting on an inflated ball, play wrestling, swinging on suspended tire inner tubes, "frog" sling swings, wet hammocks, platform swings, and "bungy" cords. Climbing and crawling over an under large pillows, beanbag chairs, jungle gyms, rocks, trees, up stairs, on hands and knees through obstacle courses made of furniture, balance activities, walking on a balance beam, rocker and wobble boards, fine motor coordination, handwriting, and peg board drawing.

A significant number of outcome studies have indicated the effectiveness of this approach to treatment along with support of Ayers [149] concept of sensory defensiveness [150-152]. In general though, OT techniques do not utilize a specific approach based on asymmetric hemispheric function or deficits.

Theories of Physical-Mechanical Interventions

The effects of physical exercise on cognitive performance

If there is one activity that seems to be the "magic bullet" against almost every disease or disorders, it is exercise, especially aerobic exercise. It seems almost every day a new study shows exercise to reduce the risk and severity of a new disease from cancer to the common cold to depression, exercise seems to be the one thing that prevents or cures them all. There have been many theories proposed as to why exercise has such dramatic health benefits. Some think it is because of its affect on heart and cardiovascular system. Some think because of its affect on the endocrine system, while others think it affects the immune system. The fact is that it affects all of these systems but aerobic exercise most impact the efficient functioning of the central nervous system. When one modality affects all of the systems of the body, it must be because of a primary affect on the brain. As we have seen, autonomic, immune, endocrine, cognitive, emotional, and sensory systems are all asymmetrically distributed in the brain. Exercise therefore must have a generalized affect on all brain functions. As we know, the primary source of activation of the brain is through the motor system, therefore, high frequency low intensity activity of the motor system will have powerful affects on the global activation, arousal, and attention of the cerebellum, thalamus, basal ganglia and cerebrum. Aerobic exercise affects all muscles of the body including the involuntary postural antigravity muscles, as well as the voluntary muscles of the extremities and trunk. It also increases the efficiency of the cardiovascular system to deliver blood and oxygen to the brain, and increases the capacity of the lungs to take in oxygen. We would expect, therefore, that exercise would be helpful in improving a child's ability to learn and control behavior and to focus attention. Lack of physical activity would be expected to cause the opposite affect.

It has been demonstrated that mice who regularly exercise on running wheels had twice the number of new brain cells compared to sedentary mice. One of the study's authors, Fred Gage, has said that, "More people in my lab have started running since we found this result." The studies

published in the Proceedings of the National Academy of Sciences and in Nature, Neuroscience [153,154] are remarkable in several ways. Gauge's laboratory demonstrated that humans along with mice and non-human primates do grow new brain cells after birth. In a previous study, the Salk researchers had found that those mice who had "enriched environment" with a tunnel, toys and an exercise wheel grew more cells than those in regular lab cages [155]. What's more, in the area of new brain cell growth, the hippocampus is associated with learning and memory. Researchers thought that it might not just be running per se, but exercise in general that causes the growth of new brain cells. Does growing more brain cells mean the running mice are necessarily smarter? Van Praag and Gauge have said it is reasonable to think so because previous studies on "enriched environment" mice showed that they perform better on learning tasks. Exercise has been shown to enhance cognitive function and to help stroke victims recover from brain injury [156,157].

The type of exercise is important and the combination of physical activity and mental focus or "purposeful" activity at the same time or close together, appear to yield the greatest changes. Nudo and associates [158] documented plastic changes in the functional topography of primary motor cortex (M1) that are generated in motor skill learning in the normal, intact primate. The investigators employed intra-cortical micro-stimulation mapping techniques to derive detailed maps of the representation of movements in the distal forelimb zone of M1 of squirrel monkeys, before and after behavioral training on two different tasks that differentially encouraged specific sets of forelimb movements. After training on a small-object retrieval task, which required skilled use of the digits, their evoked-movement digit representations expanded, whereas their evoked-movement wrist/forearm representational zones contracted. These changes were progressive and reversible. In a second motor skill exercise, a monkey pronated and supinated the forearm in a key (eyebolt)-turning task. In this case, the representation of the forearm expanded, whereas the digit representational zones contracted. Their results show that M1 is alterable by use throughout the life of an organism.

These studies also reveal that after digit training there was a real expansion of dual-response representations, that is, cortical sectors over which stimulation produced movements about two or more joints. Movement combinations that were used more frequently after training were selectively magnified in their cortical representations. This close correspondence between changes in behavioral performance and electrophysiologically defined motor representations indicates that a neurophysiological correlate of a motor skill resides in M1 for at least several days after acquisition. The finding that co-contracting muscles in the behavior come to be represented together in the cortex argues that, as in sensory cortices, temporal correlations drive emergent changes in distributed motor cortex representations.

Tantillo and associates [159] had performed a study examining the effects of exercise on children with ADHD evaluated by studying the rate of spontaneous eye blinks, the acoustic startle eye blink response (ASER), and motor impersistence. The children evaluated, both male and female, were between 8 and 12 years old all meeting the DSM-III-R criteria for ADHD. All children

in their study ceased methylphenidate medication 24 hours before and during each of three daily conditions. After a maximal treadmill walking test to determine cardio-respiratory fitness (VO(2peak)), each child was randomly assigned to counterbalanced conditions of treadmill walking at an intensity of 65-75 percent VO(2peak) or quiet rest. Responses were compared with a matched group of control participants. Boys with ADHD had increased spontaneous blink rate, decreased ASER latency, and decreased motor impersistence after maximal exercise. Girls with ADHD had increased ASER amplitude and decreased ASER latency after sub-maximal exercise. The authors findings suggest an interaction between sex and exercise intensity that is not explained by physical fitness, activity history, or selected personality attributes. Their findings support the employment of vigorous exercise programs as adjuvant in the management of the behavioral features of ADHD.

Elliot and associates [160] examined the effects of antecedent exercise conditions on maladaptive and stereotypic behaviors in 6 adults with both autism and moderate to profound mental retardation. The behaviors were observed in a controlled environment before and after exercise and non-exercise conditions. From the original group of participants, two were selected subsequently to participate in aerobic exercise immediately before performing a community-integrated vocational task. Only antecedent aerobic exercise significantly reduced maladaptive and stereotypic behaviors in the controlled setting. Neither of the less vigorous antecedent conditions did. When aerobic exercise preceded the vocational task, similar reductions were observed. There were individual differences in response to antecedent exercise. These authors note that the use of antecedent aerobic exercise to reduce maladaptive and stereotypic behaviors of adults with both autism and mental retardation is supported.

Rosenthal-Malek and Mitchell [161] reported similar results. They investigated the reduction self-stimulatory behaviors in adolescents with autism after vigorous exercise. Celiberti and colleagues [162] in a detailed case study of an autistic boy also examined the differential and temporal effects of two levels of antecedent exercise (walking versus jogging) on his self-stimulatory behavior. The exercise conditions were applied immediately before periods of academic programming. Maladaptive self-stimulatory behaviors were separately tracked, enabling identification of behaviors that were more susceptible to change (e.g., physical self-stimulation and “out of seat” behavior) versus those that were more resistant (e.g., visual self-stimulation). Examination of temporal effects indicated a decrease in physical self-stimulation and “out of seat” behavior, but only for the jogging condition. In addition, sharp reductions in these behaviors were observed immediately following the jogging intervention and gradually increased but did not return to baseline levels over a 40-minute period.

We now know that exercise has benefits for overall health as well as for cognitive function. Recent studies using organism models have been directed towards understanding the neurobiological bases of these benefits. It is now clear that voluntary exercise can increase levels of brain-derived neurotrophic factor (BDNF) and other growth factors stimulate neurogenesis,

increase resistance to brain insult, and improve learning and mental performance. Recently, high-density oligonucleotide microarray analysis has demonstrated that, in addition to increasing levels of BDNF, exercise mobilizes gene expression profiles that would be predicted to benefit brain plasticity processes. Thus, exercise can provide a simple means to maintain brain function and promote brain plasticity [163].

Lieberman and colleagues [164] reporting in the American Journal of Clinical Nutrition note that the brain requires a continuous supply of glucose to function adequately. During aerobic exercise, peripheral glucose requirements increase and carbohydrate supplementation improves physical performance. The brain's utilization of glucose also increases during aerobic exercise. However, the effects of energy supplementation on cognitive function during sustained aerobic exercise are not well characterized. The investigators examined the effects of energy supplementation, as liquid carbohydrate, on cognitive function during sustained aerobic activity. Young, healthy men were randomly assigned to 1 of 3 treatment groups. The groups received a 6 percent (by vol.) carbohydrate (35.1 kJ/kg), 12 percent (by vol.) carbohydrate (70.2 kJ/kg), or placebo beverage in 6 isovolumic doses, and all groups consumed two meals (3200 kJ). Over the 10-hour study, the subjects performed physically demanding tasks, including a 19.3-km road march and two 4.8-km runs, interspersed with rest and other activities. Wrist-worn vigilance monitors, which emitted auditory stimuli (20/h) to which the subjects responded as rapidly as possible, and a standardized self-report mood questionnaire were used to assess cognitive function. These investigators found that vigilance consistently improved with supplemental carbohydrates in a dose-related manner; the 12 percent carbohydrate group performed the best and the placebo group, the worst. Moodquestionnaire results corroborated the results from the monitors; the subjects who received carbohydrates reported less confusion, and greater vigor than did those who received the placebo. Supplemental carbohydrate beverages enhance vigilance and mood during sustained physical activity and interspersed rest. In addition, ambulatory monitoring devices can continuously assess the effects of nutritional factors on cognition as individuals conduct their daily activities or participate in experiments. These approaches have not been employed in studying neurobiological involved children.

In an interesting study reported by Thornton and associates [165], Positron Emission Tomography (PET) was used to identify the neuroanatomical correlates underlying 'central command' during imagination of exercise under hypnosis, in order to uncouple central command from peripheral feedback. Three cognitive conditions were used: imagination of freewheeling downhill on a bicycle (no change in heart rate, HR, or ventilation, V(I)), imagination of exercise, cycling uphill (increased HR by 12 percent and V(I) by 30 percent of the actual exercise response), or volitionally driven hyperventilation to match that achieved in the second condition (no change in HR). The researchers found significant activations in the right dorso-lateral prefrontal cortex, supplementary motor areas (SMA), the right premotor area (PMA), superolateral sensorimotor areas, thalamus, and bilaterally in the cerebellum. In the second condition, significant activations

were present in the SMA and in lateral sensorimotor cortical areas. The SMA/PMA, dorso-lateral prefrontal cortex, and the cerebellum are concerned with volitional motor control, including that of the respiratory muscles. The neuroanatomical areas activated suggest that a significant component of the respiratory response to 'exercise', in the absence of both movement feedback and an increase in CO2 production, can be generated by what appears to be a behavioral response.

Lardon and Polich [166] examined the electrophysiologic effects of physical exercise by comparing groups of individuals who engage in regular intensive physical exercise (12 + h/week) to control subjects (2 + h/week). Electroencephalographic (EEG) activity was recorded under eyes open/closed conditions to assess baseline differences between these groups. Spectral power was less for the exercise compared to the control group in the delta band, but greater in all other bands. Mean band frequency was higher for the exercise compared to controls in the delta, theta, and beta bands. Some differences in scalp distribution for power and frequency between the exercise and control groups were found. The findings suggest that physical exercise substantially affects resting EEG and again supports the effects of exercise on brain function.

Traditionally the view has been that there is a separation between motor skills and cognitive ability. However, the same pathways and same global increase activation of the areas involved with motor skill also underlie the areas that form the foundation of cognitive ability. However, the brain is activity dependent, therefore even though the potential to learn is enhanced through motor training, if a specific cognitive skill is not trained, it will not adequately develop.

Humans speak, they type, they sign, they write each and intricate motor skill. In the domain of music people play the fiddle, may dance to it and they may sing or hum along. People build cabinets, knit, and blow fine glassware. These diverse motor activities are beyond the realm of other organisms and suggest that motor capabilities are related to other intellectual capabilities. Indeed some psychologists such as Jerome Bruner have suggested that even human language capability is an outgrowth of capabilities involved to create new motor sequences."

"Extensive evidence suggests that knowledge is acquired as a result of extensive practice, thousands of hours of highly dedicated practice is key in separating the most successful people in various motor and non-motor skill domains from the rest of us. This perspective grew initially out of analysis of chess expertise, but also has been found to apply to muscle performance and basketball." Keele concluded, "…The surprising idea that stands out in the expertise literature is that the extraordinary motor capabilities of humans are best understood as an extension of their extraordinary cognitive abilities." When we examine "geniuses" through out history, we can see that artists and sculptors like da Vinci and Michelangelo, musicians like Bach and Mozart, were geniuses not only in their cognitive ability but also in their motor skill as well, to paint or play music."

The question is, does the constant practice of developing a motor skill like painting, or playing an instrument creates the cognitive genius or visa-versa? Motor skills develop first. We know

motor skills develop first in a child but if they focus on the motor skill to the exclusion of all else, then they will not perform well in other areas of life. However, if motor skill is used as a tool to develop brain areas, and then academic and social pursuits are diligently taught, the child will learn those activities better and faster. The key is balance and in an otherwise normal child who is behind, and in a child who is developmentally delayed, the fastest and most effective way to increase the rate of development of their brain function may be through motor activity and motor development. If there is a delay in motor skill development, then there will be a subsequent delay in their cognitive and emotional development as well.

Occupational Therapists think that hyperactive children often have persistent tonic neck reflexes. This is a normal reflex present in young children and they think that if this reflex persists in older children, it is not only a sign of poor neurological organization, but makes it difficult and uncomfortable for the child to sit normally. OT's note that many children who are hyperactive are also fidgety, sit in unusual postures, especially a slumped posture or hook their feet under the chair for support. They may tend to stand when eating or doing homework and they may experience fatigue of their neck and postural muscles, which becomes painful and affects the child's ability to concentrate. Occupational Therapists have designed a series of crawling exercises and claim that these intervention techniques are effective in alleviating the ADD symptoms and improve academic performance and behavior. These techniques emphasize the importance of the motor system to effect the neurological development of a child's brain and a subsequent improvement in learning and behavior. While the theory does not take into the cerebellum, differential hemispheric activation, and their effects on developing brain function into consideration, the theory does emphasize the role of postural muscles in the manifestation of the observed symptoms. Most children with learning disability and ADD do have poor postural tone, indicative of cerebellar, thalamic and frontal lobe dysfunction. Therefore, any activity emphasizing proximal and postural coordination will increase feedback to these brain regions. These activities may be more significant to right brain development and therefore would be expected to improve symptoms of right brain deficit, including hyperactivity, ADD, and behavioral problems.

Therapeutic Relations Between Musculoskeletal and Cognitive Function

The majority of all sensory input arises from somatosensory receptors of the musculoskeletal system and the largest percentage of that amount comes from the receptors of the spinal muscles and joints located in the upper cervical spine receptors [167]. Through the ability of these spinal receptors and based on their upright orientation and transduction of gravitational forces into electrochemical impulses that constantly bombard the brain by way of the dorsal column and spinocerebellar and non-specific thalamic pathways, they provide the baseline activation or arousal on which, in part, other brain activity is based. Through specific pathways, the same somatosensory receptors can affect specific cortical areas that are involved with higher functions of perception, cognition, and emotional behavior, especially in the frontal lobe.

However, with manifestation of symptoms, especially musculoskeletal symptoms, which make up the vast majority of health complaints of humans, they are primarily symptoms of neurological dysfunction and are best treated by effecting the nervous system directly. This can be achieved by use of spinal manipulation, joint mobilization, exercise and by stimulating the brain through a variety of environmental stimuli, such as sound, light, heat, cold, odors, tactile sensation, and cognitive activities. Virtually all those with neurobehavioral disorders of childhood also demonstrate dysfunction of their motor-sensory system. Either this dysfunction of the motor-sensory system may in fact be a primary cause of the brain dysfunction or the brain dysfunction may be the primary cause of the motor-sensory dysfunction. Either way, the motor-sensory systems, which include the postural muscles and joints of the spine and neck are dysfunctional.

Therefore, no matter what the primary source, an intervention strategy for the motor-sensory dysfunction ought to result in an improvement of brain function and vice versa. This is especially true in the frontal lobe where we have seen that both motor and non-motor functions can be measured and a dysfunction of one is reflective of an equal dysfunction of the other. Therefore, an improvement of frontal lobe motor function associated with an improvement in a child's motor function capacities, such as muscle tone, coordination, mobility, strength, and endurance, should also be reflective of an improvement in non-motor functions of the frontal lobe such as cognitive, emotional, and behavioral. By directing and including diagnosis and treatment of musculoskeletal system function, we develop tools of measuring and affecting central nervous system status.

Luoto et al., [168] examined the relationship between musculoskeletal complaints relating to higher brain function. The authors examined the mechanisms explaining the association between lower back pain and deficits in information processing. Low back trouble, chronic pain in general and depression has been associated with impaired cognitive functions and slow reaction times. It is known that the preferred hand performs significantly better than the non-preferred hand in motor tasks. The authors hypothesize that chronic low back pain hampers the functioning of short-term memory in a way that leads the preferred hand to loose its advantage over the non-preferred hand, but that the advantage would be restored during rehabilitation. Reaction times for the preferred and non-preferred upper limbs were tested in 61 healthy control and 68 low back pain patients. A multi way analysis of covariance was used to examine the group, handedness, and rehabilitation effects on reaction time. A significant interaction among group, handedness, and rehabilitation was found. At the beginning, the reaction times for the preferred hand were faster among the control subjects, but not among the patients with low back pain. After the rehabilitation, the preferred hand was faster among both the control subjects and the patients with low back trouble. During the rehabilitation, back pain, psychological distress, and general disability decreased significantly among the patients with chronic low back trouble. The results support the hypothesis that chronic low back pain and disability impedes the functioning of short-term memory, resulting in decreased speed of information processing among patients with chronic low back symptoms.

Numerous studies [169,170] report on a theory that suggests that a dysfunction in the way of the brain receives and processes information from the body, may trigger so called writer's and musician's cramps. Researchers have found that the debilitating disorder also called focal dystonia of the hands stems from pushing the brain past its ability to learn quick repetitive movements. When the brain signals become "jumbled" these researchers think the muscles spasm and stiffen. Byl and Merzenich [171] based their studies on previous research that explains the mechanism of how messages are wired to the brain. Studies explain how tactile receptors or nerves on the skin speed signals to sensory maps, which undergo rewiring or plasticity with each learning experience. We can read these maps and identify zones corresponding to individual fingers and parts of the fingertips.

According to ongoing studies conducted by Byl, Merzenich, and colleagues [171] on monkeys, rapid repetitive movements result in degeneration of the brain's sensory map that leads to muscle spasm and impaired muscle tone. They suggested that during successive movements, the brain is forced to process too numerous sensations and muscle commands. This gives rise to faulty movements they say that causes fingers and hands to spasm. Standard therapy is used to treat focal dystonia including anti-Parkinson's drugs, muscle relaxants, and injections of botulinuium toxin (Botox) to weaken problematic muscles. The authors feel that this treatment approach may be inappropriate. Instead, they suggest retraining therapy that consists of exercises to help patients fine-tune their tactile senses. This should, they think, help diffuse overloaded sensory maps so they can discriminate sensations better.

Byl noted that after 12 weeks of retraining therapy, 14 of 16 patients with severe focal dystonia of the hand who were not helped by standard therapies reported improvement in function and were able to return to work. A brain scan taken on one of the patients showed that the sensory maps appeared more neatly arranged. Although many think that there are primary biomechanical factors that produce repetitive strain type injuries, Byl thinks that focal dystonia of the hand is more likely to occur if a person is exposed to biomechanical risk factors like a high level of repetitive movements and small fingers spread. She maintains that a significant factor focal dystonia is a disorganization of the sensory maps adding that Botox and other treatments simply "quiet symptoms." She further states, "The nervous system is responsive to repetitive behaviors but we have always assumed that those modifications of the nervous system from repetitive movements would have a positive outcome, that it would make one smarter and be able to test more accurately. But what we are saying is we have identified a dysfunctional reorganization of the sensory brain that seems to be associated with the disability disorder negative outcome." Focal dystonia, as described by Byl and associates, can be considered a primary dysfunction in the motor system, including the basal ganglia, thalamus, cerebellum, and frontal lobe. Focal dystonia or hypokinetic behaviors may be isolated to the sensory-motor cortices. Lower back and neck pain are also oftentimes considered repetitive strain injuries and the same mechanism may apply. Hypermobility of the spinal joints may also produce improper repetitive sensory input that may

rewire sensory maps to produce fatigability or oxidative stress to brain cells. This may result in a focal dystonia of the spinal muscles with effects on the sensory- motor cortices. These painful muscle spasms either may be a product of the central nervous system irregular activation or may also result in abnormal repetitive feedback to the cortex.

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