Integrative Imaging in Neuroplasticity, Wisdom and Neuropsychiatry

Science Meets Arts (SMART)

By

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Preface

Neuroimaging of chess players such as grand masters and comparison to matched controls might help reveal the neuroplasticity changes in brain such as cognition and problem solving abilities. Neural underpins of behavioral data could further elucidate the neurobiological connections and the underlying neural mechanism due to training effects, especially for long-term professional practice. Also brain science including topics of cognitive function such as music/creativity training and experience as well as scientific education including mathematical calculation, learning and memory could be investigated with neuroimaging approaches that provide objective and *in vivo* imaging evidence of specific brain functional and structural neuronal resources utilization and relocation. For instance, music experience such as singing, listening, playing and professional improvisation activated several brain circuits including emotion regulation such as relief and pleasure, reward perception from anticipation to consumption, language system such as comprehension and communication as well as motor function from planning to coordination. Furthermore, for well education, college life cultivates professional skills, improves social interaction and communication, broadens vision and expands mind, gains experience and expertise and finally enriches knowledge and creativity. Emotional intelligence (EI) and general intelligence that were used for reasoning and analyzing to solve problems are usually emphasized for improvement during academic training. People with normal and high intelligence, especially superior EI ability, could perform better in complicate environment and obtain more academic achievement with successful appraisal, monitoring, utilization of emotions and social skills. Also positive effects of emotional regulation and facilitation in after-college life had showed promotions of creativity and mood in better working environment as well as enhanced interpersonal communication with better EI. Finally, watching movie paradigm with fMRI could be used to improve brain function and characterize individual variation due to different art contents, culture, background and environment. Several issues had been addressed such as session and condition differences due to the specific length and focused smooth activation patterns of movie fMRI, for the applications in neuroscience and neuropsychiatry. The beneficial effects in brain circuits involving memory and attention, reward and social values, decision making and coordination, creativity and persistence of these skills as well as expertise including chess practice, music/counting training, college education and watching-picture/movie were reviewed and investigated with full-spectrum, solid and up-to-date experimental data utilizing advanced quantitative imaging techniques in the first four chapters of this book. Associated phenotypic correlations were further illustrated to validate the training and learning imaging evidence together with anticipated neuroprotective and neurodevelopmental improvements with multiple neuroimaging modalities.

Attention-deficit and hyperactivity disorder (ADHD) is a relatively high prevalent neurodevelopmental disease, having about 6% prevalence rate worldwide. It had been reported that age and family socioeconomic status affected the prevalence of ADHD in children and adolescents, with more comorbid symptoms such as additional loss of impulsivity in adults. ADHD could be classified into the primary combined and inattentive subtypes from the typically-developed (TD) controls. Neuroimaging findings included both intra- and inter- network hyper-connectivities in ADHD group compared to TD controls, such as abnormally increased connectivities from typical functional default mode network (DMN), central executive network (CEN), salience and visual networks. Furthermore, numerous studies have been performed to investigate brain changes associated with drug addiction for better treatment and recovery effects. As another example, inverse coupling between DMN and CEN was increased after nicotine replacement pharmacotherapy, and these inter- and intra-network changes including enhanced CEN and reward systems were related to the withdrawal symptom improvement. And in the substance-dependent brain, large-scale network communication efficiency was lower via small-worldness analysis with disruption of inter-regional regulation topology, indicating possible loss of inhibition and addiction risk of drug seeking behavior. The second part of this book illustrated specific brain functional and structural changes of ADHD and drug dependence in chapters 5 and 6. In addition to multiparametric and novel imaging analysis and applications in real and relatively new database, integrative neuroscientific findings and therapeutic evaluation with neuroimaging techniques were also reviewed.

Comprehensive imaging investigation of the arts and science training effects in professionals, early college learning experience, daily skills and culture-based practice on brain were thoroughly exhibited in this new book. Expected improvements and novel functional/structural gains of brain regions and circuits in several aspects including reward/emotion/intelligence/decision making were emphasized and detailed. Brain reserve, especially the neuroplasticity and wisdom accumulation over lifetime education and intellectual activities/experience could preserve healthy cognitive-emotional structure, remain less vulnerable to functional impairments and protect against neuropsychiatric disease challenges. The aim of this new book is thus intended to provide both beginners and experts in biomedical imaging and general public health a broad and complete brain picture of positive arts and science training benefits with thorough analysis and solid data covering college education to professional expertise. Extensive applications in common diseases together with the cutting-edge and full-spectrum static and dynamic, functional and structural, regional and inter-network, imaging and phenotypic characteristics are the highlights and advantage of this book. We would hope to capture the interests of colleagues and researchers in the areas of neuroplasticity imaging, neurodevelopmental and neuropsychiatric applications as well as disease diagnosis and treatment. The ultimate goal is to convey the methodological innovation and neuroscientific applications of important education, health, arts and science-related topics. The author would also like to acknowledge the open NeuroImaging Tools & Resources Collaboratory (NITRC) database for sharing and managing the original imaging data, and especially the precious resources provided by several Chinese research branches in Chapters 1, 3 and 5.

Chapter 1 – Imaging evidence of brain cognitive and neuroplasticity changes associated with chess practicing skills and expertise had been reported. In this study, we found consistent gray matter density and interhemispheric correlation changes in chess players compared to controls, including both higher in the superior frontal, medial prefrontal cortex and visual/cerebellum regions. The VMHC identified extra hypo-connectivity in the parietal and cuneus regions but hyper-conductivity in the temporal cortex and subcortical basal ganglia and hypothalamus, while VBM localized further higher gray matter densities in the orbitofrontal, caudate, cuneus and supplementary motor areas in the chess group. These primarily increased gray matter densities and connectivity in critical brain regions indicated expected improvement of cognitive function including decision planning and making (supplementary motor and superior frontal), memory and attention (posterior temporal and orbitofrontal), visuospatial ability (occipital) and movement coordination (subcortical and cerebellum) in chess masters. In line with the structural/conductivity changes, increased intra- and inter-network connectivities of several crucial brain networks were identified, including visual network (VN), central executive network (CEN), thalamocortical circuits such as motor network (MN), default mode network (DMN)-medial frontal region, frontoparietal network (FPN) as well as the salience network (SN) in the chess players compared to controls. Increased dynamic correlations of typical brain networks such as VN, CEN, MN and DMN/CEN together with longer dwell time/occupancy/frequency for optimal strategy in chess players had also been confirmed. Moreover, global neural activity and regional synchrony signals were enhanced in chess professionals compared to controls, together with the higher absolute local efficiency for faster local neural source utilization.

Multiple brain activity/connectivity and phenotypic data had been revealed in chess group mostly. For instance, associations were observed between Raven's RPM score and neural activity in the superior frontal and posterior cingulate region as well as between Raven's score and gray matter density in the temporal and occipital clusters. Professional rate correlated positively with cerebellar regional synchrony, while starting age was negatively related to the interhemispheric conductivity in the salience network and temporal/cuneus region. Some other correlations existed such as positive correlations between levels and frontal VMHC, between start age and subcortical ReHo/fALFF, possibly due to neuroprotective and compensative mechanisms. Finally, consistent whole-brain voxel-wise and regional tract-specific DTI FA increments were present in chess group, including the arcuate fasciculus, inferior longitudinal and inferior fronto-occipital fascicle, corpus callosum and cortico-spinal tract. Tight links between DTI FA together with diffusivity (AD/RD/MD) metrics and phenotypic data were discovered as well, including between bilateral inferior longitudinal fasciculus/cingulum diffusivity/FA and training time/professional level in chess group. Our comprehensive results complemented previous findings, validating the multi-level (static and dynamic, local and global, structural and functional) brain quantitative gains in chess training and cognitive practice.

Chapter 2 – In this work, we had performed all six conditional VMHC comparisons, including each of three task conditions vs. resting state, as well as between two-task comparisons. Similar brain patterns of lower VMHC in the visual, temporal and somatosensory, motor areas in music/counting/memory conditions compared to resting state were observed. Between-comparisons for each two of three tasks further demonstrated the distinct regional allocation of neural resources under three conditions, including medial prefrontal, anterior cingulate, insular, superior temporal, occipital, thalamus, cerebellum and motor/supplementary motor areas related to music singing condition, with more differences comparing music to counting than memory conditions. The counting condition revealed more orbitofrontal interhemispheric correlation in addition to specific intra-parietal sulcus (IPS) and superior frontal gyrus (SFG) conductivity compared to music/memory. While clusters in the medial temporal lobe including hippocampus and parahippocampus, posterior cingulate, precuneus, dorsolateral prefrontal cortex (DLPFC) and superior parietal lobe maintained higher VMHC during episodic memory recall processing than music and counting tasks.

Functional connectivity based ICA-DR algorithm identified enhanced network connectivities of intra- DMN, FPN and SN during music singing condition compared to counting and memory recall tasks. On the other hand, lower inter-network connectivities including inter- DMN and FPN, frontal and temporal network (FTN) were observed due to possible neural source shifting and deactivation. Higher intra- and inter- FPN, VN, FTN, VN-DMN and

SN network connectivities in counting condition compared to music and memory tasks were discovered, consistent with the hyper-connectivity of IPS/SFG/DLPFC VMHC values. Finally, as expected, more connection of intra- and inter- temporal, DMN-FPN, FTN and thalamo-cortical circuit were present during episodic memory recall condition. The dFNC connectogram confirmed the higher temporal dynamics of six representative networks such as higher DMN-CEN-MN connections at three task conditions compared to resting state. Small-worldness analysis revealed slightly higher global but lower local efficiencies in counting and music conditions together with relatively higher small-worldness weighting factor in the memory condition compared to resting state. Our multimodal neuroimaging results were consistent with published findings for each separate condition, and provided extra imaging evidence of arts and science training-related neuroplasticity and dynamic modulation enhancement in brain structure and function.

Chapter 3 – The objectives of this chapter were to investigate the brain changes such as neural activity and myelin-related functional correlation as well as morphological/microstructural connectivity-based neuroplasticity improvements during college training with baseline and longitudinal imaging and phenotypic data. For the fALFF correlational results, several regions presented significantly positive correlations between fALFF neural activities and four aspects of emotional intelligence (EI) scores including insula, hypothalamus, cuneus and motor areas at all three time points. Longitudinally, increased associations between fALFF and EI scores were observed in the visuospatial regions and frontal medial/dorso-lateral portions. For trait association, fALFF neural activities in some similar regions such as frontal, motor/supplementary motor areas, thalamus, basal ganglia and temporoparietal regions also presented negative association with different aspects of the trait scores at three time points. For the ReHo associations, EI scores including all four aspects were positively associated with regional homogeneity in the parietal/superior temporal cluster and premotor/motor areas. During all the three time points, Raven's CRT score was positively associated with ReHo values in the orbitofrontal and superior frontal, insular, superior temporal and motor/supplementary motor areas. For the VMHC, significant longitudinal increments in the inferior temporal area, posterior cingulate and inferior parietal regions were observed. VMHC values in the cerebellum, temporal cortex including hippocampus/parahippocampus and superior segment, sensorimotor area and occipital/parietal lobes showed consistently negative associations with the depression/anxiety scores.

Significant positive correlations between gray matter density in the cerebellum, insular, orbitofrontal, fusiform, cuneus, posterior cingulate, medial prefrontal, subcortical caudate and putamen regions were observed with the EI scores of four domains including appraisal, monitoring, social ability and utilization at three time points. While cortical temporal regions including hippocampus and parahippocampus, orbitofrontal and superior frontal, visual and sensorimotor areas demonstrated significant correlations and predictions with depression and trait/state anxiety scores mainly. Associations between EI/trait scores and DTI FA/diffusivities in several tracts of the thalamic radiation, splenium of corpus callosum, internal capsule, cingulum, superior longitudinal fasciculus and cortico-spinal tract were identified at all time points. Finally, significantly increased global and decreased local efficiencies longitudinally were identified, indicating a more optimal and efficient brain network topology at later time point after college training. In line with the results presented in previous Chapters 1 and 2, these brain regions showed improvements of neural activity, synchrony and integration, myelin-related conductivity, morphological and microstructural connectivity for better performance and achievement with skills training, emotional and social interaction as well as knowledge accumulation.

Chapter 4 – The purpose of this chapter was to investigate both longitudinal session and conditional effects of fMRI paradigm including movie and flankers stimulation on brain, as well as the associated phenotypical correlations. With ICA-DR algorithm, both session and conditional effects were observed. For instance, during movie-watching, session-differences were reflected in the regions of medial orbitofrontal cortex, medial and superior frontal, middle temporal gyrus, inferior parietal lobe, angular gyrus, motor/premotor area and several regions in the visual cortex including subregions V1-V5, precuneus, cuneus, lingual, intracalcarine and occipital pole. Conditional network-based connectivity alterations such as movie vs. resting and inscape vs. resting comparisons involved mostly precuneus and inferior parietal gyrus. These dynamic network-based correlational changes indicated significant and specific visuo-motion enhancement of emotion/creativity/social communications related to the movie contents and brain cognitive processing. Significant functional network topological property with increased local and global network efficiencies (absolute) at later compared to earlier sessions for all conditions including movie and resting state were identified.

Significantly higher global VMHC Z-value during inscape stimulation compared to rest (P=0.02) and movie conditions (P=0.01) were observed. Global functional activity/conductivity z-value variations of each condition and session were exhibited additionally, such as relatively higher movie/inscape fALFF neural activity compared to rest/flankers conditions. Phenotypic associations were also revealed with fMRI metrics, including positive correlation between fALFF during movie watching condition and internal-state of hunger score as well as negative correlation between fALFF/VMHC global z-values during inscape stimulus and internal hunger/full scores. With dFNC connectogram analysis, similar distribution of mean dwell time of all six states in several sessions were observed with significantly lower mean dwell time in later session compared to baseline. Consistent with previous findings, our quantitative and multiparametric imaging results remained relatively consistent for different types of visual stimulations and tasks, suggesting temporal or long-term neuroplasticity and brain connectogram improvement from artistic and training paradigm such as movie and flankers.

Chapter 5 – The purposes of this chapter were to investigate further brain structural and functional changes in Attention-deficit and hyperactivity disorder (ADHD) combined (AC) and inattention (AI) subtypes compared to typically developed (TD) children with available structural and functional MRI data using multiple advanced imaging methods. For both structural gray matter density (GMD) and interhemispheric correlation, AC group presented significantly larger GMD and VMHC values compared to TD and AI, and relatively close values between AI and TD were found. Specifically, medial orbitofrontal cortex, temporal pole, anterior cingulate, cuneus and supplementary motor area presented both higher values of GDM and VMHC in AC group that might be related to the hyperactivity and attentional deficits in ADHD. Small clusters in the cerebellum, temporal and dorsolateral regions also showed atrophy in AI group compared to TD.

For functional connectivity differences with ICA-DR algorithm, reduced intra- and inter-network connectivities of posterior DMN, visuo-temporal, thalamic-occipital and fronto-temporal networks were observed in AC group compared to TD and AI. However, increased network connectivities in the visual, frontal, anterior DMN, thalamo-temporal, and anterior cingulate-FPN regions were found in AC group. Both relative local efficiency and small-worldness weighting factor were lowest in the AC group but highest in the AI group, while the absolute local and global efficiencies were abnormally highest in AC but lowest in AI group. Based on dFNC analysis, reversal dFNC connectogram patterns for most states were revealed in AC compared to TD. The mean dwell time was lower in AC compared to TD, and was significantly lower in the AI patients compared to TD group. Our quantitative multiparametric imaging results showed reliable and rigorous brain changes in ADHD and subtypes compared to TD controls.

Chapter 6 – The purposes of this chapter were to identify brain neural correlates of clinical data including drug dependence, with advanced multiparametric imaging quantification including fALFF/ReHo/VMHC, ICA-DR and dFNC. Significant negative associations between functional imaging including fALFF/ReHo/VMHC as well as intra-/inter- network functional connectivities identified with ICA-DR algorithms with phenotypic data such as dependence and time of use were identified in multiple brain regions, including the ventral striatum, insula, cerebellum, temporal cortex and orbitofrontal cortex together with hypothalamus and ventromedial prefrontal cortex. Education and handcraft experience showed some neuroprotection effects in several regions including the orbitofrontal, ventral striatum, hypothalamus, superior frontal and temporal amygdala/ hippocampus areas. Graph-theory based centrality showed significant correlations between binarized/weighted centrality degree and number of cigarettes per day as well as between weighted local functional connectivity degree centrality and number of cigarettes. Based on dFNC analysis, abnormally hyper-connectivities of connectograms in several states were identified including abnormally higher between-network dynamic correlations (close to 1) of state S4 for all the connections. The number of occurrence was relatively evenly distributed with close to mean value of 16% for all states (similar to the chess control group as in Chapter 1), while the distribution patterns of frequency and dwell time were similar to those of ADHD-AC type as illustrated in Chapter 5. Therapeutic strategies that target strengthening typical brain circuits in addiction such as CEN, DMN, SN and FPN/MN as well as thalamo-cortical connections might be effective for better brain inter-network modulation and dynamic facilitations with more regular behavior and better emotion/cognitive control.

Chapter 1
Comprehensive Imaging Findings in Professional Chess Players

Abstract

Imaging evidence of brain cognitive and neuroplasticity changes associated with chess practicing skills and expertise had been reported recently. In this study, we found consistent gray matter density and interhemispheric correlation changes in chess players compared to controls, including both higher in the superior frontal and medial prefrontal cortices as well as visual/cerebellum regions. The VMHC identified extra hypo-connectivity in the parietal and cuneus regions but hyper-conductivity in the temporal cortex and subcortical basal ganglia and hypothalamus, while VBM localized further higher gray matter densities in the orbitofrontal, caudate, cuneus and supplementary motor areas in the chess group. These primarily increased gray matter densities and connectivity in critical brain regions indicated expected improvement of cognitive function including decision planning and making (supplementary motor and superior frontal), memory and attention (posterior temporal and orbitofrontal), visuospatial ability (occipital) and movement coordination (subcortical and cerebellum) in chess masters. In line with the structural/conductivity changes, increased intra- and inter-network connectivities of several crucial brain networks were identified, including visual network (VN), central executive network (CEN), thalamocortical circuits such as motor network (MN), default mode network (DMN)-medial frontal region, frontoparietal network (FPN) as well as the salience network (SN) in the chess players compared to controls. Increased dynamic correlations of typical brain networks such as VN, MN and DMN/CEN together with longer dwell time/occupancy/frequency for optimal strategy in chess players had also been confirmed. Moreover, global neural activity and regional synchrony signals were enhanced in chess professionals compared to controls, together with the higher absolute local efficiency for faster local neural source utilization.

Multiple links between brain activity/connectivity and phenotypic data had been revealed in chess group additionally. For instance, associations were observed between Raven's RPM score and neural activity in the superior frontal and posterior cingulate region as well as between Raven's score and gray matter density in the temporal and occipital clusters. Professional rate correlated positively with cerebellar regional synchrony, while starting age was negatively related to the interhemispheric conductivity in the salience network and temporal/cuneus region. Some other correlations existed such as positive connections between levels and frontal VMHC, between start age and subcortical ReHo/fALFF, possibly due to neuroprotective and compensative mechanisms. Finally, consistent whole-brain voxel-wise and regional tract-specific DTI FA increments were present in chess group, including the arcuate fasciculus, inferior longitudinal and fronto-occipital fascicle, corpus callosum and cortico-spinal tract. Tight links between DTI FA together with diffusivity (AD/RD/MD) metrics and phenotypic data were discovered as well, including between bilateral inferior longitudinal fasciculus/cingulum diffusivity/FA and training time/professional level in chess group. Our comprehensive results complemented previous findings, validating the multi-level (static and dynamic, local and global, structural and functional) brain quantitative gains in chess training and cognitive practice.

Keywords: fMRI, chess, neuroimaging, functional connectivity, dynamic functional network correlation, functional activity, regional homogeneity, neuroplasticity, intelligence, Raven's progressive matrices score, training effects, gray matter density, interhemispheric correlation, structural connectivity, fractional anisotropy, diffusivity, attention, memory, decision making, movement coordination

1. Introduction

1.1. Overview

Chess is a board game that has long history with significant learning, training, reward and wisdom benefits in China and also the whole world. Neuroimaging of chess players including grand masters and comparison to matched controls might help reveal the neuroplasticity changes in brain such as cognition and problem solving abilities. Neural underpins of behavioral data could further elucidate the neurobiological connections and the underlying neural mechanism due to training effects, especially for long-term professional practice [1]. Based on MRI diffusion tensor imaging (DTI), increased microstructural connectivity and integrity were found in chess players, including inferior longitudinal fasciculus (ILF), superior longitudinal fasciculus (SLF), uncinate fasciculus (UF) and cingulum that had important language and memory function [2]. Also DTI diffusivity in the SLF was negatively associated with chess tournament ranking, and fractional anisotropy (FA) in several tracts including UF and ILF were correlated with Raven's progressive matrices (RPM) score for measuring fluid intelligence [2, 3]. Furthermore, better players with higher intelligence also had more efficient brain functioning, and manifested as higher event-related synchronization of cortical neural activation [4]. Superior chess skills correlated with larger memory capacity of knowledge and patterns based on memory performance tests [5].

Long-term professional training of chess playing emphasizes winning the board game with the shortest time and optimal strategy from complicate and variable dynamic patterns exchanged between two players. The improvements of visuospatial attention and contexture recognition in chess experts had been reported in several studies. For instance, salience and ventral attention networks were anatomically and functionally altered in chess masters compared to amateur players based on brain connectome [6]. Chinese chess experts were found to have thinner cortical depth (a global communication distance measure through anatomical mantle) in several brain regions for visual attention and memory, but with increased functional connectivity to distant brain regions in comparison to novices [7]. These brain changes might indicate chess experts recruited more of these regions for maximizing visuospatial information and exceptional performance [7]. Activity in the brain pattern recognition regions such as posterior temporal and left inferior parietal areas were related to the performance outcome of experts [8]. Enhanced fusiform area activation was reported in experts compared to novices in response to naturalistic full-board chess positions [9]. Finally, the collateral sulci (medial occipitotemporal) on both sides were involved in chess-specific pattern recognition while the occipitotemporal junction was linked to general object recognition in chess experts [8, 10].

Chess expertise practice sharpens long-term memory chunk to allow for quick pattern retrieval and recognition (especially at “win” situation), and these chunks were found to be located primarily in the temporal lobe together with the short-time working memory allocated in the frontal and parietal lobes [11]. Memory tests identified extensive brain activation in the frontal (e.g., medial and inferior segments) and posterior cingulate cortices as well as cerebellum in chess players [12]. In addition, left-sided temporo-parietal and frontal areas were activated with the expert archival paradigm for autobiographical memory recall [13]. Also the right temporoparietal junction (TPJ) and orbitofrontal cortex corresponded to the theory of mind to reason about other’s internal state and action rationality evaluation [14]. The TPJ region was found to play important role in complex visual configuration processing for chess experts [15]. In addition, only in the chess experts, interhemispheric correlation such as in the TPJ area was enhanced together with bilateral activation in frontoparietal and occipital regions for accurate chess position visualization [16, 17]. Furthermore, the collateral sulci linked the object position to the spatio-functional environment information stored in memory [18].

And medial prefrontal cortex (MPFC) subserved functional interactions with the amygdala and hippocampus for one's own and social hierarchy learning as well as for the purpose of self-relevant knowledge update [19]. Finally, prolonged electroencephalogram (EEG) signal of N2 and P3 peaks for executive control and selective attention functionalities in chess players were found in response to different chess targets, indicating success pattern matching and memory chunk retrieval in experts [20].

Regarding decision making and global strategy, augmented activation in the inferior parietal cortex (IPC) and lingual gyrus during visual stimulation together with higher striatum and pre-supplementary motor area (SMA) for decision-making facilitation had been reported [21, 22]. Chess masters also exhibited larger inter-striatum-default mode network (DMN) connection, possibly for goal-directed cognitive performance and theory of mind optimization [23]. On the other hand, during chess problem-solving task, DMN connectivity was deactivated but caudate-DMN connectivity was enhanced for possible better high-level cognitive support in chess masters [24]. Enhanced functional connectivity, higher regional homogeneity (ReHo) and fractional amplitude of low frequency fluctuations (fALFF) for local synchronization and neural activity biomarkers reached agreement in several brain regions including posterior fusiform that might benefit from chess expertise [25]. Also large-scale network analysis identified higher clustering coefficient and increased small-worldness properties, possibly due to the increased functional connectivity in the hippocampus/thalamus, basal ganglia and temporo-parietal regions [26]. And better dynamics including higher number of occupancies and longer dwell time in majorities of states were present in chess experts based on dynamic connectome quantification [27].

1.2. Objectives

Imaging evidence of brain cognitive and neuroplasticity changes relating to chess practicing skills and expertise had been reported. The purposes of this chapter are to 1. investigate further brain functional and micro-structural changes in professional chess players compared to controls with available fMRI and DTI data using multiple advanced imaging methods; and 2. correlate the imaging quantifications with phenotypic data in chess players using both voxel-wise and global statistical computation methods and also extend the current knowledge of neuroplasticity and wisdom gain of chess game.

2. Methods

2.1. Participants

Imaging data of 29 chess masters (including usual players) and 29 age- and education level- matched controls were recruited for this project to study brain cognitive function improvements with chess training (Table 1). Imaging and phenotypic data were downloaded after approval from the website managed at the NeuroImaging Tools & Resources Collaboratory (NITRC) database (www.nitrc.org). The multimodal MRI dataset of professional chess players were provided by the Huaxi MR Research Center (HMRRC) at West China Hospital of Sichuan University, as the INDI Prospective Data Sharing Samples hosted by NITRC (http://fcon_1000.projects.nitrc.org/indi/IndiPro.html).

Group	Age (Years)	Gender	Education	Level
Control (N=29)	25.8±1.3	15F, 52%	13.9±0.6 (Y)	4.7±0.2
Chess (N=29)	**Age**	**Gender**	**Education**	**Level**
	28.7±2.0	9F, 31%	13.3±0.5 (Y)	2.3±0.2
	Raven's RPM	**Rate**	**Starting Age**	**Training Time**
	49±1.3	2401.1±28.1	8.6±0.5 (Y)	11.4±2.3 (Y)

* Code for level scale: grand master=1; master=2; play often=3; used to play=4; only know rules =5; don't know rules and never played=6.
In the chess group, 6 grand masters were included with level =1, 11 masters with level =2, 10 players with level =3, 1 with level 4 and 1 with level 5.

Table 1. *Demographic information including age, gender and education levels of two groups as well as phenotypic data including level for amateur controls and professional level for chess group, Raven's progressive matrices (RPM) score, professional rate (in 2009 for this data), starting age of playing and training time of years for chess group.*

No significant differences of age and education levels comparing professional chess group to controls were found, and detailed statistical information of participants of two groups are listed in Table 1. In the chess player group, there were 6 grand masters and 11 masters as well as 10 usual players. There were significant correlations between professional rate and level in chess group (r=-0.670, P<0.001), also between training time and level (r=-0.523, P=0.004) as well as between Raven's progressive matrices (RPM) score and rate (r=0.501, P=0.006).

2.2. Imaging Parameters and Data Processing

MRI experiments were performed using the 3T MRI scanner with standardized imaging protocols. The 3D Magnetization-prepared rapid acquisition gradient-echo (MPRAGE) sequence was run with

TR/TI/TE=1900/900/2.3 ms, flip angle=9°, matrix size=256 x 256 x 176, resolution=1 x 1x 1 mm^3 for reference image used in resting-state (RS)-fMRI activity/connectivity/conductivity maps, as well as for structural voxel-based morphometry (VBM) analysis. For the RS-fMRI data acquired under relaxing condition, a standard gradient-echo EPI sequence (TR/TE=2000/30 msec, flip angle=90°, number of volumes=205, spatial resolution=3.75 x 3.75 x 5 mm^3) was utilized. DTI data was obtained with standard spin-echo EPI sequence (TR/TE=6800/93 msec, flip angle=90°, number of diffusion directions= 42, b-value=1000 s/mm^2, spatial resolution =1.8 x 1.8 x 3.0 mm^3).

The MRI and fMRI images were processed with the in-house developed scripts to derive the voxel-mirrored homotopic correlation (VMHC), VBM, independent component analysis-based dual regression (ICA-DR) remapped components, resting-state functional connectivity (RSFC) and fALFF maps, as described in details from our previous works [19, 20]. Between-group comparisons of quantitative post-processed images were performed with advanced statistical tools using Analysis of Functional NeuroImages (AFNI, http://afni.nimh.nih.gov) package and FMRIB Software Library (FSL, http://www.fmrib.ox.ac.uk/fsl) toolbox. Graph theory based small-worldness systematic analysis was computed to the correlation matrix generated from 116 seeds-based RSFC maps and compared to a degree-matched random network to derive both absolute and relative, local and global efficiency metrics [28, 29].

Novel dynamic functional network correlation (dFNC) connectogram and regional homogeneity (ReHo) map together with typical VMHC, ICA-DR, fALFF, and small-worldness analyses were performed to two data cohorts. The details of data processing were similar to the methods described in our recently published works

[28-31]. For instance, six typical and important functional networks were used for dFNC analysis, including default mode network (DMN), frontoparietal network (FPN), salience network (SN), motor network (MN), visual network (VN) and central executive network (CEN or EN). ReHo map was generated to reflect local synchrony of spontaneous neuronal activities spatially, after preprocessing the fMRI data such as motion correction and low-pass filtering for each voxel of the 4D fMRI data [30, 31].

DTI data were first pre-processed with the Diffusion Toolkit toolbox (http://tractvis.org) to obtain the fractional anisotropy (FA) and three diffusivity metrics such as axial diffusivity (AD), radial diffusivity (RD) and mean diffusivity (MD) values in original B0 diffusion space. For the FA/RD/AD/MD quantification, the FSL tract-based spatial statistics (TBSS) toolbox steps 1–2 (i.e. preprocessing, brain mask extraction with FA>0.1 and normalization) were used for registration of all participants' FA into the FSL 1-mm white matter skeleton template. Statistical comparisons between chess and control groups were performed to the voxel-wise whole brain and 20 tract-based FA/AD/RD/MD data. Correlations between functional and structural/micro-structural imaging data (both voxel-wise and regional/global quantification of statistical Z-values) and phenotypic scales such as professional rate, level and training time were also performed to examine any associations between neural responses and behavior/cognitive metrics [32, 33].

3. Results

VBM results showed significant higher gray matter densities (GMD) in the superior frontal, caudate, cerebellum, occipito-parietal junction, dorsal medial thalamus, supplementary motor area and small orbitofrontal clusters in chess masters compared to controls

($P<0.01$, Figure 1A), based on the T1-MPRAGE data. Moreover, higher interhemispheric correlations in the temporal, superior frontal, MPFC, visual, hypothalamus, basal ganglia and cerebellar regions were found in chess masters compared to controls ($P<0.05$, Figure 1B) with fMRI data. However, lower VMHC in the posterior cingulate, superior parietal and cuneus regions existed in chess masters as well.

Using ICA-DR algorithm, higher inter- and intra- network connectivities of visual, thalamocortical including temporal and sensory regions, DMN-MPFC, salience network-superior temporal, and superior frontal regions were present in the chess players compared to controls ($P<0.05$, Figure 2). Lower inter-network connectivities of thalamo-occipital/frontal, DMN-visual, fronto-motor and cerebellum regions existed on the other hand, for possible rerouting, deactivation and inhibition function. Also based on relatively new dFNC analysis, higher dynamic correlations between SN-CEN, SN-DMN, FPN-MN and VN-DMN of fMRI correlation matrices data existed in chess masters compared to controls at representative state S3, with relatively lower inter- MN-VN connection (Figure 3). Similar network connectivity patterns were found in both controls and chess masters in another representative state S4, with slightly higher SN-MN and FPN-VN but lower FPN-SN inter-network connectivities in chess master compared to controls. Evenly distributed cluster occurrences in all six states were present in controls (Figure 4 A1, 16-18%); while evenly distributed in five states (Figure 4 B1, 17-22%) but quite lower in one state (3%) were found in chess masters. Relatively longer mean dwell time in majorities of states was observed in chess masters compared to controls, with higher frequency found in most states as well (Figure 4; B1 and B2 respectively).

Higher global mean Z-values of ReHo, VMHC, fALFF and sub-bands S4/S5 were observed in chess master group compared to control group. Significantly higher global mean Z-values ($P<0.01$) of ReHo and fALFF sub-band S5 in chess masters compared to controls were displayed in Figure 5A, and strong correlations between global Z-values of ReHo and fALFF in chess masters including all fALFF sub-bands (S4 and S5) and conventional band (all $r>0.48$, $P<0.009$) were demonstrated in Figure 5B. No other significant voxel-wise functional homogeneity, activity or connectivity differences between chess and control groups were found with $P>0.05$. In addition, graph-theory based small-worldness analysis of the fMRI correlational data presented higher absolute local but lower relative global efficiencies in chess masters compared to control group (Figure 6A), together with slightly lower small-worldness weighting factor in chess master group (Figure 6B). Significantly higher absolute local efficiency at all sparsity levels in chess masters compared to controls were observed ($P=0.02$).

Applying statistical correlational analysis to the whole brain voxel-wise imaging data, strong associations between phenotypic scores (mainly for chess master players) and fALFF values (marker for the neuronal activity) were observed. For instance, positive correlations between starting age and fALFF values in the temporo-occipital, subcortical putamen as well as cingulate areas, between professional rate scale and fALFF in temporal/cerebellar cluster, between professional level and temporal fALFF, between Raven's RPM score and fALFF values in the posterior cingulate/precuneus and MFPC, training time and left superior parietal regions were observed (Figure 7A, $P<0.05$). Also negative correlations between rate scale and occipital fALFF, between Raven's RPM score and sensorimotor fALFF, between training time and temporal fALFF existed. For the VBM results, chess master level correlated with gray matter density (GMD) in the dorsolateral and medial prefrontal regions but linked to GMD of sensorimotor areas in control group and even negative association in the subcortical caudate region (Figure 7B, $P<0.05$). Positive correlation between GMD in occipital /temporal regions and Raven's RPM score in chess group was found. Furthermore, negative correlations between rate scale and gray matter densities in the dorsolateral prefrontal cortex, between Raven's score and basal ganglia gray matter, between training time and gray matter densities in the frontotemporal and motor areas were observed as well.

Figure 8 demonstrated the phenotypic associations with fMRI ReHo and VMHC quantification (left and right panel respectively), and mainly for chess master group with $P<0.05$. For instance, significant positive correlations between ReHo and chess professional level were exhibited in the medial/superior frontal region, and similarly for professional rate score in the small cerebellum. Starting age also correlated negatively to the regional homogeneity (ReHo) in the insular, superior temporal and premotor/motor areas, but positively to the ReHo values in the supplementary motor area, subcortical caudate and occipital cortex. Strong associations with negative correlations between Raven's RPM score and ReHo in the frontal/motor areas/small temporal clusters, between training time and superior frontal ReHo were also found (Figure 8A). For the VMHC, strong positive correlations between professional level and frontal/occipital interhemispheric correlation were identified in master group, but only frontal conductivity correlated with level scale in the control group. As expected, starting age was negatively related to VMHC in the regions of insular and superior temporal cortex (salience network), cuneus, sensorimotor and language Wernicke's and Broca's areas in chess group (Figure 8B). Moreover, Raven's RPM score correlated positively with superior temporal VMHC, and training time was linked to VMHC in large areas of frontotemporal and thalamic regions.

Based on TBSS analysis, significantly higher FA (corrected $P<0.05$) values in several brain tracts were found in chess masters compared to controls, including arcuate fasciculus, cingulum, inferior longitudinal, inferior fronto-occipital fasciculus, corpus callosum and cortico-spinal tracts (Figure 9). Significant correlations between quantitative DTI metrics including 20 tracts-specific mean FA/AD/RD/MD values and phenotypic scores in controls and mostly chess masters are illustrated in Figure 10. For instance, significant links between bilateral inferior longitudinal fasciculus diffusivity (AD/RD/MD) and training time/professional level ($|r|\geq0.48$, $P\leq0.008$) in chess group; as well as between bilateral SLF diffusivity and training time/ professional level ($|r|\geq0.48$, $P\leq0.008$) were observed. In addition, the right cingulum FA/MD values were associated with training time in chess group (($|r|\geq0.51$, $P\leq0.004$). However, FA of right cingulum connecting the hippocampus correlated positively with professional level ($r=0.50$, $P=0.006$) in controls, but radial diffusivity (RD) correlated negatively with level ($r=-0.51$, $P=0.005$; and similar to chess group). The quantitative significant correlations ($P<0.01$) are also listed in Table 2.

Tract Name	**Phenotypic Data**	**DTI**	**r**	**P**
Cingulum R	training time	FA	0.5420	0.0024
		RD	-0.5140	0.0043
Inferior longitudinal fasciculus L	professional level	MD	0.4830	0.0080
	training time	RD	-0.5480	0.0021
		MD	-0.5420	0.0024
Inferior longitudinal fasciculus R	training time	RD	-0.4850	0.0076
		AD	-0.5720	0.0012
		MD	-0.5490	0.0021
Superior longitudinal fasciculus (temporal part) L	professional level	AD	0.4840	0.0079
	training time	MD	-0.4830	0.0079
Superior longitudinal fasciculus (temporal part) R	professional level	MD	0.4970	0.0061
	training time		-0.5210	0.0037
Forceps major	*professional level in controls*	*FA*	*0.4970*	*0.0061*
Cingulum (hippocampus) R		*RD*	*-0.5100*	*0.0047*

Table 2. *Significant correlations (P<0.01) between phenotypic data and DTI tracts with four metrics of DTI (FA, MD, AD and RD) and 20 tracts in chess group (first 12 rows) and control group (last two rows). L=left, R=right.*