INTERNATIONAL CONFERENCE ON EDUCATIONAL NEUROSCIENCE

Abu Dhabi, United Arab Emirates - February 28-29, 2016
The purpose of the International Conference on Educational Neuroscience is to bridge the gap between education and neuroscience. It offers an outstanding venue for neuroscientists, educationalists, and psychologists to present emerging science in the field of brain, mind and education, learn from experts, collaborate with peers, and to explore new tools and technologies. Specifically, the scope of the conference is to discuss and explore up-to-date research in developmental neuroscience, cognitive neuroscience, brain plasticity and learning, and how neuroscience findings can be informative for educational practice, including language processing, reading, mathematics, and several other learning-related cognitive processes.

Talk sessions encompassed areas of neuroscience that carry implications for education, including brain plasticity, development, and learning, with leading researchers from across the world invited to give talks. Posters covered various cellular, developmental, and functional topics, including changes in health on brain structure, and on cognitive function, effects of perceptual content on task completion and brain activity, bilingual language processing, neurodegeneration, neuronal plasticity, the monitoring of mathematical skills in an educational setting, and the importance of identifying systemic brain biomarkers for learning difficulties.

Brain Products, NIRx, and C&P International kindly sponsored part of the event and provided equipment, software, and licenses, for the practical sessions, which were essential for the EEG and fNIRS data collection sessions. MagVenture also provided equipment and software for the TMS practical session.
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Greeting and opening words

Prof. Robert Milne
Acting Vice Chancellor of ECAE.

Ladies and gentlemen, good morning.
Thank you all for coming, and welcome to Abu Dhabi!

Emirates College for Advanced Education (ECAE) in the United Arab Emirates organized its first International Conference on Educational Neuroscience over the 28th – 29th February 2016 that included a workshop with hands-on experience in data collection of simultaneous EEG and fNIRS recordings using Brain products Acticap and NIRx’s Scout systems. ECAE is the sole dedicated Educational College in Abu Dhabi and it supports conferences whose topics have an impact on education in this region and internationally. It is also starting Ed D and PhD programs including one on Educational Neuroscience.

The conference was designed to present a broad view of the current achievements in the areas where education and neuroscience overlap with particular emphasis on the latest neuroimaging tools and technologies.

I confess to no expertise in the area of educational neuroscience but I want to convey my excitement at being a spectator of this emerging field of human endeavor.

Up until now, educational theories have been mostly dependent on social science studies – collecting data on numerous subjects and trying to correlate student outcomes with various external inputs. In this approach, it is extremely difficult to make conclusive conclusions due to the number of parameters and different initial conditions – enough to give an ex-physicist like me nightmares just thinking about it!

For example, there is still considerable debate about the best way to teach children to read. Part of the difficulty in determining the answer is that that people use their brains in different ways, they can have different learning styles, such as visual or aural, so there may not be a particular method that suits everyone.
Beyond teaching, how do we explain the reason for the natural talents that people possess – some have an innate ability to play musical instruments or learn extra languages while others grasp mathematical and scientific concepts easily. In extreme cases, there are a few individuals who can perform incredible calculations; giving the square root of an arbitrary number to X significant figures or giving the day of the week for a random date on the Gregorian calendar – how do they do it? [Maybe calculate is incorrect, perhaps they have some vast look-up table in their brain or some other method?]

What we need is a scientific approach to understanding how the brain works, one that can describe the causality between stimulus and reaction. Neuroscience is that approach. We are currently at the early stages of this new discipline and it is very exciting to consider how it will develop. We can already identify some genetic effects and are discovering how the brain is wired and the function of neural networks but there are still a lot of unknowns. It will take considerable effort over a long time, it will require new scientific instrumentation to be developed and it will require new theories to be proposed and tested against experimental results but eventually we will gain a much greater understanding of how the brain works and use that knowledge to improve the education of future generations.

Where will this work eventually take us? It is dangerous to try and predict the future but perhaps neuroscience will provide the key to answering one of mankind’s greatest questions – what is consciousness?

I want to extend my thanks to the team at ECAE who put in many hours organizing the conference. This was the first conference in the region integrating education and neuroscience and it was truly international with over 30% of participants coming from outside the UAE. Feedback was overwhelmingly positive and the second conference will be larger and even more successful than this first one. The abstracts printed here demonstrate the quality and scope of the papers presented and ECAE looks forward to welcoming, in 2017, all who are interested in this exciting and rapidly developing area of research – from students to world experts working in education, health and neuroscience.
I wish you a very successful meeting!
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# Program

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| 11:00 - 11:50 | Mapping the brain to harness the mind: Using behavioural and imaging data to inform educational practice  
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UAE University, UAE |
| 11:50 - 12:40 | Electrophysiological signatures of learning in the hippocampus  
Dr. Miriam Nokia  
University of Jyväskylä, Finland |
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Dr. Diogo Almeida  
New York University, Abu Dhabi |
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Speakers

**Dr. Kerry Lee**

*National Institute of Education, Singapore*

Age related differences in the influences of domain-general and domain-specific variables on mathematical achievement

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**Dr. Miriam Nokia**

*University of Jyväskylä, Finland*

Electrophysiological signatures of learning in the hippocampus

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**Dr. Diogo Almeida**

*New York University, Abu Dhabi*

Neuromagnetic investigations of lexical access

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**Dr. Hellmuth Obrig**

*Max Planck Institute, Germany*

Acquiring and applying phonological regularities during language acquisition: evidence from combined EEG and fNIRS measurements
Dr. Maurice Ptito

*Université de Montréal, Canada*

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Transcranial magnetic stimulation of the visual cortex in congenital blindness

Dr. Sam Wass

*Cambridge University, U.K.*

*University of East London, U.K.*

Learning and the autonomic nervous system: understanding interactions between states, concentration and learning during early childhood

Dr. Sami Boudelaa

*UAE University, UAE*

Mapping the brain to harness the mind: Using behavioural and imaging data to inform educational practice

Dr. Sid Kouider

*Ecole Normale Supérieure, Paris, France*

Using EEG to track consciousness, surprise and metacognition in the infant brain
Transcranial magnetic stimulation of the visual cortex in congenital blindness

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\textbf{Introduction:} For human and non-human primates, vision is one of the most privileged sensory channels used to interact with the environment. The importance of vision is strongly embedded in the organization of the brain as about one-third of its cortical surface is involved in visual functions. It is therefore not surprising that the absence of vision from birth, or the loss of vision later in life, has huge consequences, both anatomically and functionally. We have shown in previous studies that, although, the visual system is largely atrophied by the loss of vision at birth, it is nonetheless present and can be activated by a variety of non-visual stimuli, such as touch, audition, and even smell. We present here a series of behavioral and brain imaging studies showing that the congenitally blind brain is capable of cross-modal plasticity and sensory substitution.

\textbf{Methods and results:} We recently showed that the occipital lobe of blind individuals is reduced in volume (whole brain Voxel Based Morphometry-VBM) (Ptito et al., 2008) has an increased cortical thickness (FreeSurfer and CIVET) and shows a supra-metabolic activity as revealed by fluoro-desoxy-glucose (18FDG-PET) (Kupers and Ptito, 2014) (Figures 1). Moreover, other non-visual structures in the blind brain

\textbf{FIGURE 1:} Structural and metabolic changes in the congenitally blind brain.
were affected by early visual deprivation such as the posterior part of the right hippocampus (Chebat et al., 2007) and the splenium of the corpus callosum (Tomaiuolo et al., 2014), both regions showing a volumetric reduction.

**FIGURE 2:** The tongue display unit (TDU).
We used, in a series of experiments, a sensory substitution device coined the Tongue Display Unit or TDU. This apparatus translates an image grabbed by a camera into electrotactile pulses administered to the tongue via a grid of electrodes (Figure 2).

Congenitally blind (CB) subjects equipped with the TDU can learn to discriminate the orientation of a bar, discriminate motion, and shapes (Ptito et al., 2009, 2012; Matteau et al., 2010). To do so, they activate regions of the brain that are visual in nature, namely, the visual cortex and the ventral and dorsal streams as revealed with functional Resonance Imaging (Figure 1) [reviewed in Kupers and Ptito (2014)]. Moreover, the TDU has been successfully used as a navigation tool. CB individuals were able to point to recognize and avoid obstacles while walking in a corridor (Chebat et al., 2011). Tested in an fMRI scanner in a virtual route recognition task, CB participants recruited not only their visual cortex but also the parahippocampal region, areas usually activated during topographical learning and spatial representation in sighted subjects (Kupers et al., 2010). To test for the functional role of visual cortical areas in blind, we used trans-cranial magnetic stimulation (TMS). Short repetitive TMS bursts applied over the mid-occipital cortex of the blind interfere with repetition priming effects of a list of words presented several times. Moreover, rTMS over the motion cortical area, which is part of the dorsal visual stream (area hMT+), induces an increase in the reaction times to moving stimuli in blind subjects only. We tested for the subjective experience associated with the activation of the visual cortex. While control seeing-subjects experienced visual phosphenes, blind participants reported parasthesiae (tingling sensations) either on the tongue or the fingers (Figure 3). Finally, using somesthesic evoked potentials following learning with the TDU, we were able to show that the information originating

**FIGURE 3:** TMS of the occipital cortex of blind subjects can induce tactile sensations referred to the tongue (A) and fingers (B).
in area SI was transferred to the primary visual cortex of the blind through increased cortico-cortical projections.

**Conclusion:** The results obtained from this series of studies have valuable information on the nature of the plastic processes that take place in early blindness and might lead to the development of a new multisensory device that will use non-visual modalities to funnel sensory information to the visual cortex of the blind and help them “see.”

**Keywords:** blindness, vision disorders, transcranial magnetic stimulation, neuroimaging (anatomic and functional), sensory substitution device

**ACKNOWLEDGEMENTS**

The authors are indebted to these Foundations for their generous support: the Harland Sanders Foundation (Canada), the Lundbeck Foundation (Denmark), and the Danish Medical Research Council FSS, Denmark.

**REFERENCES**


Age-related differences in the influences of domain-general and domain-specific variables on mathematical achievement

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Previous studies showed that success in mathematics is dependent on both domain-general cognitive capabilities and domain-specific competencies. What remains unclear is the extent to which associations vary with age and the extent to which the relative importance of domain-general versus domain-specific factors vary. In this talk, I will focus largely on working memory and updating as representative of domain-general capacities. The extant literature point to three ways in which patterns of relations between working memory, updating, and math performance can be characterised. Studies conducted with younger children, in particular, suggest that working memory predicts mathematical performance more consistently than does prior mathematical performance. Others suggest that the explanatory power of working memory and updating is largely mediated by prior mathematical achievement. A third possibility is a dynamic model, which specifies that the relative importance of WM, updating, and prior mathematical performance vary both with age and the domain of mathematics under consideration. We tested these hypotheses with data from a 4-year longitudinal study that involved 673 children from K2, Grades 2, 4, and 6 (5, 7, 9, and 11 years old, respectively). Each year, children completed a battery of working memory (Listening Recall, Mr. X, and an updating task) and mathematics tasks. For mathematics, we adopted both a wider lens that examined the development of mathematical skills in general and a narrower lens that focused on the development of algebraic skills. The former was measured using a standardised math task (Numerical Operations). The latter was measured using both mathematical relation tasks (Number Sequences, Function Machine, Functions) and algebra word problems. Examination of concurrent relationships indicated that the magnitude of relations between Numerical Operations and working memory was lowest in Kindergarten, peaked at Grade 1, and moderated but remained strong for the older children. Of interest was that from a predictive perspective, working memory predicted performance on Numerical Operations equally well across the 10 grades. In contrast, compared to the primary years, performance in the more senior grades was more heavily dependent on performance the year before. Despite strong cross-sectional correlations, working memory and updating did not consistently predict performances on any of the mathematical relational or algebraic tasks. Interestingly, children with smaller working memory and updating capacities in 7th grades tended to do better in 8th grade algebra. The canonical relation (i.e., higher
capacity, better performance) was observed again 1 year later. These findings point to a dynamic relation in which associations between domain-general, domain-specific, and mathematics performance vary depending both on grade and the domain of mathematics under consideration. It was surprising that working memory and updating failed to predict performance in algebra problems in subsequent years. This is discussed in terms of resources required for solving versus learning how to solve algebraic problems.

**Keywords:** longitudinal studies, mathematics, working memory capacity, algebra, mathematical patterns

Mapping the brain to harness the mind: using behavioural and imaging data to inform educational practice

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The interest of neuro-cognitive research in the study of Modern Standard Arabic in particular and Arabic dialects in general has grown reasonably, if slowly, over the last decade. To date, there is a descent body of work attempting not only to describe the cognitive processes underlying spoken and written word recognition in Arabic but also to explain how these processes interface with the neural architecture subserving them. In spite of this, however, classroom practice in the Arab world continues to be impervious to the insights provided by neuro-cognitive research. In this presentation, I will summarize the major findings from three research strands I have been developing in collaboration with other colleagues over the past few years. The first strand of research is behavioural and one of its major insights is that both spoken and written word recognition in Arabic are significantly modulated by the morphological structure of the word with morphemic components, in particular, roots and word patterns playing the role of cognitive units used to access and organize the mental lexicon. The second line of research, based on electrophysiological measurements of brain activity as it unfolds overtime, suggests that roots are represented in bilateral fronto-central areas and have an earlier time course than word patterns which are represented in the perisylvian areas on the left. The final strand comes from fMRI research and suggests that the ubiquitous morphological complexity of Arabic words due to the presence of a root and a word pattern strongly engages the superior and middle temporal gyri bilaterally as well as the inferior frontal gyrus on the left. These results make a compelling case for the need to focus on the morphological domain by linking word form to structure and by increasing morphological awareness among learners (and instructors) in order to build a more effective teaching practice of Arabic.

Keywords: EEG, fMRI, priming, Arabic morphology, educational practice

Electrophysiological signatures of learning in the hippocampus

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Background: Hippocampal electrophysiological activity in awake rats and rabbits is characterized by alternating epochs of rhythmic activity at the theta band (3–12 Hz) and the occurrence of sharp wave-ripple complexes (SPW-Rs, 100–250 Hz). Theta is most commonly present during voluntary movement (running) and in anticipation of external events such as when the smell of a predator is present. By contrast, SPW-Rs mostly take place during immobility. Both theta and ripples are linked to learning and memory: according to the so-called two-stage model (Buzsáki, 1989), theta is indicative of a state in which information arriving from the neocortex is encoded into hippocampal neuronal networks by granule cells. SPW-Rs, on the other hand, are initiated during the following rest periods in the hippocampal CA3 and result in synchronous firing of thousands of pyramidal cells in the CA1. It is thought that SPW-Rs result in information transfer from the hippocampus back to the neocortex for long-term memory storage.

Goals: For several years, our group has been focused on finding out how spontaneously occurring theta and ripples affect associative learning.

Methods: We use classical eyeblink conditioning as a model of associative learning. In this task, a warning signal (conditioned stimulus) is presented first, followed by an unpleasant stimulation of the eyelid (unconditioned stimulus). The unconditioned stimulus always elicits an eyeblink, the unconditioned response. As a result of repeated presentations of the conditioned stimulus paired with the unconditioned stimulus, the conditioned stimulus alone starts to elicit an eyeblink. This is called the conditioned response. During eyeblink conditioning in rats and rabbits, we record hippocampal electrophysiological activity, namely, the extracellular local-field potential (LFP) reflecting the summed synaptic currents of thousands of cells in the vicinity of the recording electrode. From the LFP, we then detect certain events on-line, for example, the occurrence of SPW-Rs, and further use this information to align the presentation of the external stimuli, for example, the conditioned stimulus. A 10-s example of LFP recorded from the CA1 pyramidal layer of the hippocampus in an awake, restrained rabbit is shown in Figure 1.
**Results**: Our work so far indicates that both theta and SPW-Rs can be used to regulate learning rate: the state in which SPW-Rs take place appears to support associative learning and hinder extinction (Nokia et al., 2010). By contrast, the state in which theta is prominent seems to promote extinction (Nokia and Wikgren, 2014). Furthermore, ongoing hippocampal theta seems to disrupt associative learning if the conditioned stimulus is timed to start at a certain phase of the oscillation (Nokia et al., 2015).

**Conclusion**: Based on our work so far, it is clear that there are many possibilities for neural markers to be used in the regulation of associative learning and extinction. Theta and SPW-Rs are easily detected by the naked eye from the LFP but other, more complex measures, such as coherence of electrophysiological activity in brain regions, of choice could just as well be used. A future challenge will be to find ways to extend our results to use in humans.

**Keywords**: hippocampus, theta oscillations, eyeblink classical conditioning, ripples, SPW-R

**ACKNOWLEDGEMENT**

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Learning and the autonomic nervous system: understanding interactions between stress, concentration and learning during early childhood

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Predominant accounts explaining links between early looking behavior and later cognitive outcomes emphasize static individual differences in information encoding; however, work from Aston-Jones and colleagues suggests that looking behavior may be dynamically influenced by ongoing, phasic changes in autonomic arousal. To test the Aston-Jones model, a 20-min testing battery constituting mixed photos and cartoon clips was shown to 53 typical 12 months old. Look duration was recorded to index attention, and continuous changes in arousal were tracked by measuring heart rate, electrodermal activity, and movement levels. Across three analyses, we found that continuous changes in arousal tracked simultaneous changes in attention measures, as predicted by the Aston Jones model. We also found that changes in arousal tended to precede (occur before) subsequent changes in attention. In a second study, we investigated causal interactions between attention and arousal by applying, over a 2-week training period, targeted cognitive training to a cohort of 12-month-old infants, aimed at strengthening the voluntary control of visual attention. Before and after training, and relative to an active control group, infants’ attentional control capacity and autonomic arousal were measured. Training was found to lead to marked changes in infants’ behaviour, across a number of different tasks, but infants’ autonomic arousal was unchanged following training. Changes in autonomic arousal remained as predictive of looking behaviour after training, as before. This suggests that arousal and voluntary attention control have separable influences on looking behaviour in infants. In the third study, we examined whether infants with more labile (sensitive) autonomic arousal patterns showed better, or worse, performance on learning tasks. Previous research has suggested that acute stress attenuates frontal lobe functioning and increases distractibility while enhancing subcortical processes in both human and non-human animals (Arnsten, 1998). To date, however, these relations have not been examined for their potential effects in developing populations. We examined the relationship between stress reactivity (infants’ heart rate response to watching videos of another child crying) and infant performance on measures of looking duration and visual recognition memory. Our findings indicate that infants with increased stress
reactivity showed shorter look durations and more novelty preference. Thus, stress appears to lead to a faster, more stimulus-ready attentional profile in infants. Additional work is required to assess potential negative consequences of stimulus responsivity, such as decreased focus or distractibility.

**Keywords:** arousal, attention, learning, infancy, stress, concentration

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REFERENCES


Using EEG to track consciousness, surprise, and metacognition in the infant brain

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My talk will focus on whether and how infants (1) experience perceptual consciousness, (2) rely on Bayesian inference during perception, and (3) rely on metacognitive sensitivity to track their own behaviors. I will first describe how one can test for perceptual consciousness in infants by relying on neural signatures of consciousness validated in adult populations. Our studies confirm the presence of these neural signatures in 5- to 15-month-old infants, but also show that such mechanisms are much slower than in adults, and accelerate throughout development. Regarding predictive coding, we combined EEG recordings with a cross-modal cueing paradigm and show that, consistent with Bayesian accounts of perception, neural responses for unexpected events are increased in 12-month-old infants. However, in infants, this effect of prediction error was observed only during late processing stages and involves the same neural signature as found for perceptual consciousness. Early neural components, by contrast, revealed an amplification for predicted rather than surprising events, suggesting that selective attention enhances perceptual processing for expected events. These results demonstrate that the neural mechanisms underlying the use of predictive signals are already functional in infancy, but follow different dynamics depending on whether expected events are confirmed or instead surprising. Furthermore, they reveal a privileged link between prediction error and consciousness in infants. Regarding metacognition, we demonstrate that infants reflect upon their own (simple) decisions to evaluate their accuracy and adapt subsequent behavior. We show that after performing a binary choice, 12- and 18-month-old infants display appropriate decision confidence by persisting more following correct as compared to incorrect decisions, even though nothing in the external world provides information about their accuracy. Furthermore, we found that an electrophysiological marker of error detection, the error-related negativity, is elicited when 12-month-old infants make an incorrect decision. Hence, although explicit forms of metacognition might mature later during childhood, the mechanisms responsible for metacognitive sensitivity are already functional during the first year of life. I will conclude on perspectives for learning and education.

Keywords: brain, consciousness, learning, EEG, infants, metacognition

Neuromagnetic and psycholinguistic investigations of lexical access: how can cognitive science contribute to education research on literacy?

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Visual word recognition is a domain of inquiry that interests cognitive scientists and education researchers alike, and it is one of the basic skills involved in literacy. I will present recent work done in the domain of visual word recognition using MEG that attempts to find reliable indices of successful lexical retrieval in brain data and discuss the potential applications of findings like these in literacy research. Namely, I will suggest that some of the findings in the cognitive neuroscience of visual word recognition may provide new insights and diagnostic tools to researchers interested in evaluating the quality and trajectory of literacy acquisition, both in neurotypical and special populations. I will also present recent psycholinguistic work done in visual word recognition in Arabic, which indicates that the end state of the acquisition of literacy may exhibit substantial qualitative cross-linguistic variation. This variation stems largely from particularities of different writing systems and their mapping to linguistic representations. If correct, this conclusion presents a potential challenge to the use of language-independent metrics to gage the acquisition of literacy in educational settings.

**Keywords:** psycholinguistics, MEG, lexical access, literacy, Arabic

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Acquiring and applying phonological regularities during language acquisition: evidence from combined EEG and fNIRS measurements

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Long before, infants produce their first words, and they acquire rules and regularities of their native language(s). This applies to all linguistic levels including phonology. Besides the phoneme inventory of the given language infants need to learn the combinatorial rules, which govern the phonological “well-formedness” of an utterance. In other words, whether or not a string of phoneemes could be an entry in the lexicon to be acquired (e.g., /BROP/ might be an English word but /TLOP/ contains an “illegal” consonant onset cluster). Apart from aiding word access, acquisition of the “phonological grammar” (phonotactics) helps to meet another important challenge. Since human speakers do not pause between each word, phonotactic rules help to segment the continuous auditory stream into potentially meaningful “chunks.” In a number of experiments, we investigated how phonotactic rules are processed, how processing changes with exposure, and how infants acquire these regularities. I will present an overview with a focus on early language development, based on studies using the combination of EEG and functional Near Infrared Spectroscopy (NIRS).

Keywords: EEG, NIRS, brain imaging, language development, phonology

The neural basis of partial reinforcement

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The partial reinforcement extinction effect (PREE) is a seemingly paradoxical phenomenon in human and animal learning in which the omission of reinforcement during the acquisition of conditioning produces an increase in conditioned responding during extinction. This phenomenon suggests that in human learning, partial reinforcement would result in more efficient learning and more stable learning. The biology that underpins partial reinforcement is poorly understood. I will describe experiments in an animal model of PREE in which we have tested the effect of partial reinforcement (100 and 50% reinforcement) on fear learning using Pavlovian Fear Conditioning. We have tested the impact of partial reinforcement on learning, and then used cell biology and electrophysiological recordings to understand the cellular changes that underpin PREE. Immunohistochemical analysis revealed increased labelling of p-ERK and c-fos in central and basolateral amygdala, hippocampus, medial prefrontal cortex, auditory cortex, and somatosensory cortex that correlated with freezing. Using in vivo multi-unit microelectrode recording revealed that the size of the PREE depended on oscillatory activity in amygdala and subiculum, particularly in the theta/alpha band (8–10 Hz). The magnitude of the PREE was also related to the synchronization of LFP oscillatory activity between BLA and subiculum. In human subjects neural activity was measured using 64 channel EEG. Behavioural responses to an explicit task were made with keyboard presses. Heart rate, respiration rate, and skin conductance responses (SCR) were measured continually throughout the experiment to index both conditioned and unconditioned responses. A within-subject design was implemented, with acquisition and extinction occurring in a single session. The conditions included 100%, random 50% and alternating (i.e., non-random) 50% reinforcement. Crucially, the random 50% condition showed greater resistance to extinction than the 100% or alternating 50% conditions. Increased conditioned responding (SCR and heart rate increases) in the 50% condition was associated with increased power in the EEG theta band (5–10 Hz). The results of these experiments revealed several novel findings: (1) a PREE was observed in both Wistar rats and humans using similar auditory CS-shock US fear conditioning protocols; (2) the PREE was demonstrated to be context sensitive: it could effectively be abolished by extinguishing in a different context to acquisition; (3) the PREE correlated with neural activity in amygdala, hippocampus, medial prefrontal cortex, auditory cortex, and somatosensory cortex; (4) the magnitude of the PREE correlated with synchronized oscillatory activity between amygdala and hippocampus (subiculum). These results suggest that partial reinforcement learning results within a Bayesian predictive coding model of brain function.
**Keywords:** amygdala, auditory cortex, cell biology, hippocampus, learning, somatosensory cortex, c-fos, medial prefrontal cortex, animal model, p-ERK, electrophysiological recordings, *in vivo* multi-unit microelectrode recording, partial reinforcement extinction effect

Age of acquisition of the second language modulates structural and functional dynamics of bilingual reading

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Neuroimaging evidence has suggested the involvement of left-lateralized perisylvian regions in reading processes (Turkeltaub et al., 2002). By contrast, research on bilingualism has showed contradictory evidence in regard to the differential involvement of language-related brain regions and networks for reading in the native (L1) and second language (L2) (Hernandez et al., 2015). This highlights the relevance of investigating in a systematic manner the main factors modulating the differential involvement of reading regions and networks in bilinguals, while controlling other potential sources of variance. The age-of-acquisition (AoA) of the L2 and language proficiency has been pointed out as critical variables that can determine potential differences in brain function and structure among bilingual readers (Klein et al., 2014). Here, we sought to investigate the effects of the L2 AoA on the function and structure of language-related regions associated with L1 and L2 reading, while controlling language proficiency and exposition to L1 and L2. To this end, we followed a multimodal neuroimaging approach examining fMRI, cortical thickness, and tractography measures in a sample of early and late bilinguals. Thirty-six bilinguals with Spanish as their L1, who learned Basque as their L2 before age 3 (early bilinguals) or after age 6 (late bilinguals), participated. All participants were high-proficient in both languages. In the scanner, they performed two separate tasks during which they were asked to press a button when they saw a colored letter within a given string (perceptual-task) or when they saw an animal word (semantic-task). Whole-brain fMRI analysis reveals no differences between groups. Region-of-interest analysis revealed a similar recruitment of left and right language-related regions in both early and late bilinguals except for the left and right pars triangularis. As compared to late bilinguals, early bilinguals exhibited a different pattern of left triangularis engagement in the interaction between task and language effects. Similarly, early bilinguals showed a more selective recruitment for word versus pseudoword reading in right triangularis. Moreover, functional connectivity analyses confirmed a tighter coactivation among left and right pars triangularis in early, but not in late, bilinguals for reading in L1 relative to reading in L2. Importantly, structural analysis revealed increased cortical thickness in right pars triangularis for early relative to late bilinguals. Additionally, enhanced functional activation for
L2–L1 language effects in the left triangularis predicted cortical thinning in their right triangularis counterpart only in early bilinguals. Finally, diffusion MR tractography of the connecting left and right pars triangularis also revealed differences between early and late bilinguals. In sum, our results indicate that the early exposure to two languages led to a more distributed involvement of regions beyond the classical left perisylvian areas in reading. Our findings provide the strongest converging evidence so far of structural and functional changes involving left and right triangularis as a result of L2 AoA in bilingual readers.

**Keywords:** language, bilingualism, DTI, fMRI, reading

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Towards systemic and individualized brain markers for learning difficulties

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Variability in brain function is meaningful: it is known that there is a wide variation in learning ability: some individuals learn quickly, others struggle in a specific domain, and others have difficulties to learn in all domains. It is also known that there are many ways to learn, and each individual can rely on a different learning strategy that best matches his/her skills, expectations, and prior knowledge. The sources of such differences in individual learning preference are not all well understood, including genetic and environmental factors. Both genetic and environmental factors inter-interact at every level, which makes their impact on learning very difficult to predict (Parasuraman and Jiang, 2012). Put another way, there is no single gene or environmental factor that taken alone would predict whether an individual is a good or a poor learner (Frith, 2011). However, what we know is that the interaction “genetic-by-environment” also leaves its signature on the individual’s brain, because it constantly shapes and modifies the brain. In this context, cognitive neuroscience and functional neuroimaging can play a pivotal role in characterising and quantifying such individual differences in brain structure and function, with the aim of identifying credible biological factors that can be related to individual differences in behaviour (Miller et al., 2012). We argue here that this cannot be achieved until a shift is made in how between-subject variability is treated in multi-subject neuroimaging studies: effects of interest are commonly expressed as mean main effects that focus on what is consistent over subjects. In this framework, variance is treated as patternless and meaningless noise, and any individual contribution that deviate from the group is ignored, down-weighted, or even penalised. We argue that this framework is too reductionist, because it does not read enough into the rich neuroimaging and behavioural data. Specifically, it is important to treat inter-individual variability as data rather than noise (Thompson-Schill et al., 2005) because it can reflect the different learning preferences or cognitive strategies that each individual adopts to reach a particular outcome (Friston and Price, 2011). Researchers can then model variability between subjects in an informed way and work out how to decode such variability to make credible predictions about the most likely learning preference or strategy used by a given individual (Seghier and Price, 2009). This framework can boost the translational potential of functional neuroimaging findings in education.
Heterogeneity in abnormal processing: one potential implication is the identification of brain markers of learning difficulties that are applicable at the individual level. There is a broad literature about abnormal processing in subjects with impaired learning such as dyslexia or dyscalculia; however, the majority of these studies were mainly concerned with average/mean effects in the population/group, and thus, we do not know the level at which those average effects are representative of the individual pattern. To derive credible characterisations of abnormal processing at the individual level, we must have a better understanding and accurate characterisation of the size of variance in normal processing. Put another way, to understand what constitutes atypical processing, we must first understand what can be considered as typical processing (i.e., estimation of the typical range of normal processing). The practical implication of the latter is to acknowledge that typical versus atypical processing may not be a categorical distinction with clear-cut thresholds; instead, they are both on the same continuous dimension of the full spectrum of learning and cognitive processing. This leads to another important observation that groups are most likely heterogeneous, with, for instance, the existence of different kinds of abnormal processing (e.g., different types of dyslexia).

Brain markers of impaired learning at the individual level: the long-term goal is to build models with credible explanatory power, that is, the possibility to generate accurate predictions about individual learning abilities that are educationally useful. First, we must recognize that there is no single brain region or connection that makes an individual a good or a poor learner. Biomarkers must therefore be expressed at the system level. Second, we must acknowledge that the brain is constantly changing, and this time-dependent brain plasticity needs to be characterized and accounted for in current models. Third, when an individual is classified as a poor learner, this does not necessarily mean that this particular individual cannot learn. To the contrary, it means that this particular individual may struggle to learn through standard means but can be advised to adopt alternative learning strategies that rely on alternative intact brain processing pathways and not his/her abnormal ones (Seghier et al., 2012). This possibility is of great importance in the educational setting because it explicitly acknowledges that learning or educational difficulties may also have a biological basis, beyond parents’ or teachers’ control (Frith, 2011), which motivates the search for alternative teaching methods that can be tailored to the individual specific needs (e.g., using technology-based learning tools).

Conclusion: We need to take every opportunity to bridge the gap between neuroscience and education. Neuroscience evidence can play a role in designing efficient teaching methods that appreciate how the brain processes information. On the other hand, neuroscience findings need to go beyond aggregate or average effects and start paying attention to the individual effect because individual differences could reflect the multitude of ways by which the brain learns and the different processing pathways that support each of those learning preferences. When an individual struggles with
learning in one way, neuroscience can advise on the most efficient alternative, based on the available processing pathways in that individual.

**Keywords:** education, learning, variability, cognitive neuroscience, brain plasticity

**REFERENCES**


Building peace one brain at a time; how education and neurosciences can help us deal with stress and trauma

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Although most people will encounter at least one traumatic event over their lifetime, via primary or secondary exposure, not all of them will develop post-traumatic stress disorder (PTSD). With the contemporary rise in violence and traumatic sources (especially, but not only, in our Arab part of the world) the World Health Organization recent reports describe PTSD as an increasing global health issue, due to its high frequency, severity, comorbidity, and cost. Similar to other mental health problems, much remains unknown about PTSD. Yet, similar to other anxiety disorders, it is marked by excessive fear. It thus comes as no surprise that the most prevalent hypothesis in PTSD is that of a fear-processing deficit. Untreated trauma seems to be the missing link in the vicious cycle of violence begetting violence in 80% of reported studies. PTSD is marked by intrusive memories (flashback, nightmares) exaggerated physiological response (sweating, increased heart rate, and altered sleep) and impaired emotional responding. It severely alters personal and professional well-being. Eye movement desensitization and reprocessing (EMDR) is the recommended first line psychotherapy. It is a novel, efficient, rapid, and long-lasting approach that shows great promise for our patients. We have reproduced that PTSD is characterized by abnormal brain structure and function. Amygdala hyperactivity alongside decreased prefrontal activity is in fact its main trademark. To the best of our knowledge, it is the first time a causal relation is further established in PTSD putting the amygdala activity at the core of the disorder. We show that increased amygdala activity causes difficulty in disengaging attention from threat cues subsequently causing anxious symptomatology. Traumatized brains are biased by the amygdala to be constantly on the lookout for threat. Most importantly, we have also shown that after symptom removal by EMDR, peripheral and central processing and grey matter density are restored. EMDR improves psychological, behavioral, and brain-based indices. On the other hand, we have looked at resilience as a protective factor to stress. It is defined as the ability to cope effectively in stressful situations and involves the ability to experience emotions matching environmental demands. We show its scores are positively correlated with right amygdala and left (OFC)! Exactly, the structures altered in PTSD. Better understanding the neural underpinnings of resilience and
mobilizing adequate emotion regulation resources is essential in advocating adaptive ways of dealing with adversities, notably in an Arab world relegating emotions to the back seat. With all this from the neurosciences, it remains a common responsibility to work on implementing adequate educational programs to help our kids foster resilience and later manage their stress and trauma exposure. Psychological interventions would thus actively participate in promoting sustainable peace, one individual brain at a time.

**Keywords:** amygdala, prefrontal cortex, fMRI, peace, post-traumatic stress disorder, resilience, eye movement desensitization and reprocessing

**REFERENCES**


Re-innervation of learning with neuronal plasticity: the neuromuscular junction as a model

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One of the most unique and intriguing qualities of the nervous system is neuronal remodeling. This phenomenon not only allows neurons to thrive and adapt to new environments but also improves their performance over time. Neural plasticity plays a key role in functionally restructuring parts of the brain based on our experiences and helps us to improve performance in important brain functions, such as learning and memory (Bailey et al., 2015). The neuromuscular junction (NMJ) serves as a useful model for investigating neural plasticity because of its simplicity, accessibility, and wealth of available background information. Identifying how synaptic structure and function change in response to use and disuse, with development across the lifespan, sheds light on synaptic turnover (Nanou et al., 2016). Remodeling of the NMJ occurs throughout the lifespan, as evidenced by its recurrent degeneration and regeneration (Fahim, 1997). Generally, aging may lead to a decrease in the number and conduction velocity of fast motor units (Krutki et al., 2015), whereas the relationship between pre- and postsynaptic components of the NMJ remains constant throughout aging (Deschenes et al., 2013). However, activity allows for modulation. For example, age-related variations in physical activity have been shown to dynamically modify the structure and function of the NMJ (Fahim, 1997), along with the coupling of muscular excitation–contraction (Fahim and Robbins, 1986). In addition, muscle strength and protein turnover increase after exercise in older subjects (Mero et al, 2013), and interestingly, the amount of damage and capacity for repair are similar for younger and older adults after strenuous exercise (Kuruganti et al., 2005). In summary, much of the reductions in functional capacity and quality of life observed in aging, are most likely the result of a sedentary lifestyle (Makanae and Fujita, 2015) and not aging per se, as corroborated by the positive effects of physical activity on muscle fibers in the elderly (Miller et al., 2014). Taken together, this highlights the relationship between experience and neuronal plasticity and emphasizes the importance of practice to sustain and improve neural function. This approach is particularly useful to better understand how learning changes neuronal plasticity in various populations, such as persons with special needs, and across age.

Keywords: exercise, aging neuroscience, NMJ, learning and plasticity, disuse atrophy
REFERENCES


Whole exome sequencing reveals complex inheritance patterns and identifies two gene mutations implicated in the development of autism and intellectual disability in a consanguineous Palestinian family

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Despite significant heritability of autism spectrum disorders (ASDs) and intellectual disability (ID), their extreme genetic heterogeneity has proven challenging for gene discovery. The application of next generation sequencing technologies to study families with complex consanguinity proved beneficial in identifying inherited risk alleles. In this study, we apply whole exome sequencing (WES) followed by segregation analysis and phenotype–genotype correlation to study genetic changes in three siblings of a highly consanguineous Palestinian family in which parents are first cousins, and consanguineous marriages ran over the past four generations. The three siblings presented with a neurodevelopmental phenotype that was evident in early childhood. One of the children presented with stereotypic repetitive behaviour suggestive of ASD and mild visual impairment. The second child presented with mild to moderate forms of ID and mild visual impairment, and the third child presented with the most severe phenotype including severe visual impairment, severe ID, and stereotypic and repetitive behaviours suggestive of ASD. WES was performed for a single child, who had the most severe phenotype presenting with both ID and ASD. WES analysis revealed the presence of two homozygous pathogenic mutations. One in the gene encoding for the cyclin M2 (CNNM2), responsible for dominant hypomagnesemia, and the second in the transmembrane TMEM-163 gene. Segregation analysis in other family members confirmed that the other two affected children with the less severe phenotype had homozygous CNNM2 mutation, but not TMEM163 mutation. The parents were heterozygous for the two gene mutations. Our results confirm that CNNM2, which was previously implicated in dominant isolated hypomagnesemia, is now causing a variable neurodevelopmental phenotype including ASD and ID when inherited in an autosomal recessive manner. The detected novel mutation is not located in the cystathionine beta synthase (CBS) domain, which is altered in structure in the dominant hypomagnesemia phenotype (Stuiver et al., 2011). Crystallography experiments indicate its possible role in changing...
the orientation of this domain rather than its direct structure. Taking into account, the normal Magnesium blood levels in our patients, and gene expression pattern of this gene in perinatal rodent brain, our data strongly suggests a new function of this membrane protein in the developing CNS. TMEM-163 protein, or synaptic vesicle 31 (SV31), was first identified by proteomics of rodent brain synaptosomes (Burré et al., 2007). Recently, it is reported to interact with the channel TRPML1, mutated in Mucolipidosis type IV patients (Cuajungco et al., 2014). Gene expression experiments revealed the expression of this gene in peri-natal rodent brain, which suggest its possible role in neural circuit development and maturation. Altogether, our data describe two novel genes and mutations implicated in severe neuropsychiatric diseases, including ID and ASD. Additionally, the use of WES technology for disease-causing gene mutation discovery has a great advantage in revealing complex inheritance patterns including the inheritance of two autosomal recessive gene mutations in the same patient and family, highlighting the role of this discovery in proper patient management and family counselling.

**Keywords:** intellectual disability, autism spectrum disorders, genetic mutation, whole exome sequencing, recessive inheritance

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**REFERENCES**


Perceptual decision-making and its implication for effective communication in education

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Background and goals: The information that we perceive from our environment is used for comprehending our surroundings and to make decisions on how to interact with it in a multitude of contexts. These brain operations, based on sensory information, constitute perceptual decision-making. In an educational setting, perceptual decisions are made whenever information appears, and understanding how to present materials, so that they fit best with the brain’s representations, allows for more effective communication and easier integration. Perceptual decision-making assessed along an easy–difficult continuum has typically been evaluated using stimulus visibility or new rule application. With stimulus visibility, weakly-visible images are more difficult to discern, and for new rule application, perceptual categories must be learned. However, most of the information that we use in our environment is highly visible and does not require learning new perceptual categorization rules. Little is known of the effect of perceptual content on how easily perceptual information is used in decision-making, and more specifically, of perceptual decisions for ecological, clearly visible stimuli. Perceptual decisions, or discrimination, for highly visible stimuli can become difficult for observers because of two main factors: (1) perceptual information can vary in the amount, or complexity, of its content (complexity) and (2) the perceptual information that must be discerned can be highly similar or dissimilar (similarity). The purpose of this work is to evaluate how perceptual content along the dimensions of complexity and similarity interact, when making decisions for highly visible information, using psychophysics and fMRI.

Methods: Participants consisted of 12 right-handed healthy adults (age range 24–35 years, mean 28.4 ± 0.95 SE). Stimuli consisted of two Gabor patches (windowed sinusoidal grating) appearing side-by-side. To manipulate complexity, carrier gratings were shown in the same orientation (simpler information) or in different orthogonal orientations (more complex information). To manipulate similarity, the line width
(spatial frequency) of the patterns ranged from highly different (easy) to highly similar (difficult). Participants were asked to specify which of the two patterns contained the higher spatial-frequency (narrower lines). Gabor patches were presented side-by-side and remained on-screen until participant response. Behavioral session: the method of constant stimuli with a 2-alternative forced-choice was used to measure spatial-frequency discrimination thresholds, expressed as Weber fractions for differences in spatial frequency. Scanning: in a mixed-design, Gabor pairs were shown at multiples of discrimination threshold to span a perceptually equivalent range of dissimilarity to similarity, for both same-orientation and different-orientation conditions.

**Results:** General. Psychophysical results indicate that spatial frequency discrimination thresholds, expressed as Weber fractions, are higher (worse performance) for different-orientation condition (0.077 ± 0.0077 SE) than for same-orientation condition (0.054 ± 0.0043 SE). fMRI results indicate that when comparing information complexity globally, for different-orientation vs. same-orientation conditions, significant activation appeared mainly in visual cortical regions. Stimulus similarity/discriminability: same-orientation (low-complexity) and different-orientation (high-complexity) conditions displayed somewhat-similar patterns, with less discriminable stimuli yielding significant activation in bilateral visual occipital regions and supplementary eye fields, and in regions supporting task-control and decision-making, including the anterior cingulate cortex, ventrolateral prefrontal cortex, and superior parietal lobule. In addition, the right inferior parietal lobule activated only for the different-orientation condition. In contrast, higher discriminability (easier), yielded significant activity in the IPL bilaterally and in the right angular gyrus, which is involved in perceptual feature saliency and spatial cognition. However, complexity and similarity interacted to yield stronger activations in monitoring and attentional regions (anterior cingulate cortex and ventrolateral prefrontal cortex) than in lower visual regions.

**Conclusion:** When similar images are used in perceptual decision-making, a small change in visual complexity can lead to a large change in brain activity with more elaborate patterns of activation, even for clearly visible images. This suggests that the way in which information is presented can lead to brain processing that is easier or more difficult. Understanding the rules by which the brain uses less demanding processing to simply perceive information and use it, allows us to build effective tools for optimal communication.

**Keywords:** decision-making, perception, fMRI, cognitive neuroscience, difficulty level
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Introduction: There is growing interest in the neuroimaging community to implement methods that can derive robust systemic explanations of brain function (Sporns, 2014). Dynamic causal modelling (DCM) (Friston et al., 2003) is a generative model that can make mechanistic explanations of brain activation at the neuronal level. Likewise, graph theoretic analysis can characterize network architecture with complex measures, such as characteristic path length, modularity, centrality, and network resilience (Rubinov and Sporns, 2010). However, DCM typically deals with subgraphs with a small number of nodes, whereas graph theory analyses rest upon the statistics on a relatively large number of edges. Recently, it has been shown that it is possible to invert large DCMs (i.e., 20-node models) that can then be submitted to graph theory and related analyses (Seghier and Friston, 2013). Here, we investigate in a systematic way how to compute meaningful graph theoretic measures from very large DCM models. Specifically, we aim to examine many methodological issues that can impact on how DCM output is fed to graph theory.

Methods: The possibility to combine DCM and graph theory raises many practical challenges, including (i) how to invert very large DCMs, (ii) how to transform (reduce) very large DCMs into useful sparse model structures, (iii) how to convert DCM connectivity parameters into quantities that can be read by graph theory, and (iv) how to make inferences at the group level. Here, we used fMRI data from six subjects during overt reading [for more details, see Parker Jones et al. (2013)]. In each subject, timeseries were extracted at \( n = 40 \) regions (nodes) that were activated during reading aloud. In each subject, a single densely-connected model was specified without modulatory parameters (B-matrix was empty), yielding models with 1,336 edges (A-matrix), a subset of edges with low anatomical priors having been excluded. All first-level, second-level, and DCM analyses were carried out with SPM12. Here, we run DCM12 with the following options: deterministic, one-state equation per node, bilinear, and mean-centered inputs.

Results: (1) Inversion of large DCMs: the computational time required to invert large models grows exponentially with the number of free parameters. The Bayesian inversion of our 40-node models was done using constrained priors that bound the number of
effective-free parameters as detailed in (Seghier and Friston, 2013). This allowed the inversion of very large models to be done in a reasonable time (i.e., around 41–78 EM iterations per model). (2) Bayesian model reduction: the inverted 40-node models were then reduced using post hoc model optimization (Friston et al., 2011). This procedure allows the reduction of a dense or even fully-connected model by assessing the impact of absent edges or connections (i.e., discover the sparsity structure) in a graph that best explains the observed time-series. The optimized structure of the reduced model at the group level was computed using Bayesian parameter averaging over our six subjects. Although group effects were assessed here during model reduction, it is possible to perform group inferences at later stages (e.g., on the DCM parameters or even after graph theory analyses). (3) DCM matrices: DCM estimates different parameters depending on the inversion scheme (e.g., deterministic, stochastic, or non-linear). Here, we limited our analyses to between-node endogenous connectivity parameters that are stored in the A-matrix. If modulatory parameters are also of interest, users can estimate total effectiveness connectivity at each edge by adding B-matrix to A-matrix. Self-connections (diagonal of the A-matrix) were ignored. (4) Generate an adjacency matrix: sparse binary undirected networks are widely used in graph theory analysis. It is possible to generate such networks by thresholding and then symmetrizing the posterior probabilities of the connectivity parameters. It is also possible to generate different types of networks depending on the question of interest. For instance, it is possible to generate binary-directed networks (e.g., binarized posterior probabilities after thresholding), weighted-directed networks (e.g., posterior expectations in the A-matrix), or weighted-undirected networks [e.g., by taking the maximum between the absolute coupling parameters of a given connection in the A-matrix and its reciprocal connection, cf. Seghier and Friston (2013)]. (5) Measures of network topology: we estimated many complex measures of centrality and modularity using graph theoretic analyses depending on the network type (Bullmore and Sporns, 2009; Rubinov and Sporns, 2010).

**Conclusion**: Here, we investigate the possibility to combine DCM with graph theory. Our aim is to provide a multi-step procedure that can be used in future studies to analyze task-free or task-induced fMRI activations. Some of the steps detailed above can be achieved using different schemes, for instance, spectral DCM to speed up model inversion when dealing with resting-state fMRI data (Razi et al., 2015), and group-based Bayesian reduction schemes for multi-subject datasets (Friston et al., 2016). We hope that the ability to invert large DCMs, in an efficient way, will provide a new opportunity for analyses using graph theory.

**Keywords**: fMRI, effective connectivity, networks, connectivity analysis, graph theory, dynamic causal modeling
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The future of transcranial magnetic stimulation in neuroscience in the Middle East

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Transcranial magnetic stimulation (TMS) is a non-invasive technique for brain stimulation, which is often used in neuroscientific research in order to investigate neural excitability and connectivity in the human brain. Recent studies have shown that the application of TMS has the potential to provoke changes in the physiological processing of the human brain. Brain stimulation is produced by generating a brief, high-intensity magnetic field by passing a brief electric current through a magnetic coil which is placed over a cortical area of interest. TMS induces modifications in neural excitability in the target area, which in turn changes the physiological processing in the brain. TMS has proven to be a valuable asset, not only in diagnostics but also for treatment of many neurological disorders, for instance, post-stroke motor deficits, depression, epilepsy, autism, and Parkinson’s disease. Of additional interest are studies which have shown that the effects of TMS can be modulated by combining TMS with pharmacological treatment. In this review, we focus on clinical TMS research and outline the results of most recent studies. Furthermore, we discuss the new potential for treatment of neurological diseases and rehabilitation purposes using TMS. With special consideration to the Middle East, we illustrate the possibilities that TMS could bring for clinicians and patients in this nationally prioritized research field.

Keywords: Middle East, transcranial magnetic stimulation, neuroscience, brain plasticity, brain stimulation

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Preclinical assessment of clinic ready compounds for the treatment of spinal muscular atrophy

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Background: Spinal muscle atrophy (SMA) is an autosomal recessive neurodegenerative disease, which is characterized by the loss of α motor neurons, resulting in progressive muscle atrophy (Mercuri et al., 2007). The loss of functional Survival motor neuron (SMN) protein due to mutations or deletion in the SMN1 gene is the cause of SMA (Lefebvre et al., 1995).

Method: A potential treatment strategy for SMA is to upregulate levels of the SMN protein originating from the copy gene SMN2, which could compensate in part for the absence of the functional SMN1 gene (Lorson et al., 2010; Faraz Tariq Farooq and MacKenzie, 2013; Faraz Farooq, 2015).

Goal of the study and results: We have shown a novel therapeutic strategy for SMA treatment through the activation of the p38 and STAT5 kinase pathway activating clinic ready compounds (Farooq et al., 2009, 2011). Celecoxib (p38 activating drug) and prolactin (STAT5 activator) demonstrate a clear promise for use in SMA clinical trial studies as they increase SMN protein levels, ameliorate disease phenotype in SMA mouse model, have blood–brain barrier penetration and also have FDA approved status (Farooq et al., 2011; 2013). We have also identified other clinic ready STAT5 and p38 pathway activators as new candidates for SMA treatment (Duncan MacKenzie et al., 2014; Hadwen et al., 2014). These results provide evidence and need for FDA approved compound library screen to identify clinic ready compounds for the treatment of SMA.

Conclusion: SMA is a deadly neurodegenerative disease with a prevalence of 1:10,000 mostly affecting children and more than 50% affected children die before the age of 2 (Feldkotter et al., 2002; Ogino et al., 2002; Ogino et al., 2004; Pearn, 1978; Roberts et al., 1970; Sugarman et al., 2012). It is the most common genetic cause of infant death and is currently untreatable (Roberts et al., 1970). This study will help in the identification of clinic ready compounds as new candidates for SMA treatment which will provide us an excellent platform to extend this approach on a wider scale to other rare disorders. We believe it shall bring effective treatments closer to reality for rare genetic disorders.
Keywords: neurodegenerative disease, neuromuscular disease, SMA, orphan drugs, kinase pathway

REFERENCES


**Tumor necrosis factor alpha in kainic acid-induced neurodegeneration**

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**Introduction:** Excitotoxicity and oxidative stress are largely considered as common pathway of cellular injury in many human acute and chronic neurodegenerative diseases, including ischemia, Alzheimer’s disease, and Parkinson disease (Nassiri-Asl et al., 2013; Doble, 1999). Tumor necrosis factor alpha (TNF-α) is a proinflammatory cytokine with homeostatic and pathophysiological roles in the central nervous system (CNS) (Sriram and O’Callaghan, 2007). It was shown that mice lacking TNF receptor-1 (TNFR1) exhibit greater neurodegeneration in kainic acid (KA)-induced neurotoxicity, suggesting that TNF-α exerts its protective role via TNFR1 (Lu et al., 2008). The nerve growth factor (NGF) is involved primarily in the growth, maintenance, proliferation, and survival of neurons. Insulin-like growth factor-I (IGF-I) protects neurons against a wide range of injuries (Zhang et al., 2008). The objective of the present study is to investigate the role of TNF-α on KA-induced neurotoxicity at several time points in order to find out the possible mechanisms underlying its effects.

**Methodology:** TNF-α knockout (KO) and wild-type (WT) C57BL/6 male mice (6–8 weeks old) were partially anesthetized with Isofluen and given KA dissolved in water (10 mg/1.3 ml) intranasally at a dose of 40 mg/kg bodyweight (Chen et al., 2002). Mice were sacrificed, and hippocampi were dissected and kept in liquid nitrogen. Protein extraction is performed in T-PER tissue protein extraction reagent. Levels of glutathione (GSH), malondialdehyde (MDA), β-NGF, and IGF-I were assessed by ELISA using commercially available kits. For immunohistochemistry, mice were anesthetized, transcardially perfused, brains fixed, and sectioned. Frozen hippocampal sections were exposed to rabbit anti-glial fibrillary acidic protein (GFAP) for astrocytes and rabbit antihumanized calcium binding adaptor molecule-1 (Iba-1) (Lu et al., 2008).

**Results:** KA induces seizures in all the mice; however, TNF-α KO mice showed more severe and long-lasting seizures (Figure 1). KA also produced oxidative stress in both strains represented by increased levels of MDA 30 min post KA administration. However, the MDA levels were significantly higher in TNF-α KO mice 1 day post KA treatment compared to Wt-mice (Figure 2A). The Wt-mice showed a compensatory mechanism by increasing the levels of GSH 1 and 3 days post KA treatment. However, the TNF-α KO mice failed to compensate and the GSH stores were depleted (Figure 2B). Levels of IGF-I in hippocampal supernatants were significantly reduced in TNF-α KO KO mice.
mice 30 min and 4 h post KA treatment, while it is reduced in Wt mice 4 h post KA treatment then returned to its normal levels (Figure 3A). Levels of β-NGF remained unchanged in Wt mice, while it is significantly elevated in TNF-α KO mice (Figure 3B).
KA resulted in increased expression of both GFAP and Iba-1 in the hippocampi of both groups; however, the expression was significantly higher in the TNF-α KO mice than in the Wt-mice (Figure 4). Interestingly, astrogliosis and microglial activation were evident for up to 1 month after KA treatment, especially in TNF-α KO mice with high seizure scores.

**Conclusion**: TNF-α deficiency worsens KA-induced neurotoxicity, as evident by more severe seizure activity, severe oxidative stress, depletion of GSH, reduced levels of IGF-I, induction of β-NGF as compensation to the severe damage, and prolonged astrogliosis and more activated microgliia.

**Keywords**: astrocytes, kainic acid, microglia, oxidative stress, NGF, TNF-α

**REFERENCES**


Reducing cognitive load in educational and multimedia learning environments

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Multimedia learning environments are commonly used in teaching and learning. They have the potential in presenting the information in various formats. However, research studies found that the use of multimedia learning environments in teaching and learning is not always effective. They may impose heavy cognitive load on learners, which cause working memory overload and, therefore, hinder learning. This ineffectiveness may result from inappropriate design of multimedia instruction, which overloads working memory and results in ineffective learning. One of the reasons for this working memory overload is the split attention effect that occurs when learners need to mentally integrate two related sources of information at the same time in order for the learning materials to be understood. For example, one of the approaches of reducing split attention in multimedia learning environments is using visual cues (attention directing cues) to guide students’ attention as a try to reduce split attention and therefore enhance learning. The use of visual cues reduces visual search and thus reduces the cognitive load on students’ working memory. This poster presents different approaches to design multimedia learning environments in a way that reduces split attention. In addition, this poster will report the results of a research study that used three different types of visual cueing in multimedia instruction to found out which learning environment significantly reduced split attention measured by a mental effort scale. The participants of the study are pre-service teachers in one of the teacher training colleges. The participants were equally divided to three different treatment groups. The three groups were exposed to the same multimedia learning environments that vary only in the cueing strategy that was implemented. This study used Quasi-experimental design. Results indicated that using the cueing strategy that did not block the related content in the multimedia learning environment significantly reduced split attention comparing to the other different cues.

Keywords: multimedia, cueing, working memory training, cognitive load, split attention effect

REFERENCES


Hippocampal neuroinflammation, neurodegeneration, gliosis in Wistar rats following adrenal gland removal

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Bilateral adrenalectomy has been shown to damage the hippocampal neurons (Adem et al., 1994; Gould et al., 1990; Sloviter et al., 1989). Although the effects of long-term adrenalectomy have been studied extensively, there are few publications on the effects of short-term adrenalectomy. The relation between the neuronal cell death that occurred in such neurodegenerative model and the inflammatory response in the hippocampus at the early stages has not been examined. In the present study, we aimed to investigate the effects of short-term bilateral adrenalectomy on the levels of pro-inflammatory cytokines IL-1β, IL-6, and TNF-α, neurodegeneration and the response of microglia and astrocytes to neuronal cell death over the course of time (4 h, 24 h, 3 days, 1 week, and 2 weeks) in the hippocampus of Wistar rats. Our results showed a transient significant elevation of pro-inflammatory cytokines IL-1β and IL-6 from 4 h to 3 days in the adrenalectomized rats compared to sham-operated rats. After 1 week, the elevation of both cytokines returns to the sham levels. Surprisingly, TNF-α levels were significantly elevated at 4 h only in adrenalectomized compared to sham-operated rats. In order to investigate the time line of neuronal cell death occurrence, a Fluoro-Jade B staining was performed and our results showed a time-dependent increase in degenerated neurons in the upper blade of the dentate gyrus from 3 days to 1 week after adrenalectomy. After 2 weeks of adrenalectomy, we observed a progression of cell death throughout the upper blade of the dentate gyrus. The activation of microglia and astrocytes is one of the major response to the neuronal death, our results revealed an early activation of microglia on day 3, whereas activation of astroglia in the hippocampus was observed at 1 week postoperatively. A progression of microglia and astroglia activation all over the dentate gyrus and their appearance for the first time in CA3 of adrenalectomized rats hippocampi compared to sham-operated rats was seen after 2 weeks of surgery. Our study showed an early increase in the pro-inflammatory cytokines followed by neurodegeneration and activation of glial cells. Taking these findings together, it could be suggested that the early inflammatory components might contribute to the
initiation of the biological cascade responsible for subsequent neuronal death in the current neurodegenerative animal model. These findings suggest that inflammatory mechanisms precede neurodegeneration and glial activation. It could be speculated that in several neurodegenerative diseases, such as Alzheimer’s disease, chronic adrenal hormones increase, and/or their receptors’ decrease result in inflammatory mechanisms which lead to hippocampal neurodegeneration (Heuser and Lammers, 2003; Landfield, 1978; Landfield et al., 1978; McEwen, 1997; Woulfe et al., 2002).

**Keywords:** adrenalectomy, hippocampus, neurodegeneration, neuroinflammation, microgliosis

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**REFERENCES**


Cognitive activation in mathematics lessons: links to mathematics interest, self-efficacy, and achievement

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There are growing concerns among educational policymakers and practitioners over the dwindling numbers of students choosing to study STEM subjects, such as science, technology, engineering, and mathematics. As a result, education systems across the world have been “frantically” exploring ways to foster students’ interest in STEM subjects and to encourage them to pursue a career in STEM-related fields. Of the STEM subjects, mathematics cuts across the other three subjects, and a high-level of content mastery in mathematics is considered indispensable to success in STEM-related careers. The present study, therefore, drawing on data from the fifth cycle of the Program for International Student Assessment (PISA) examined the relations of cognitive activation in mathematics lessons to mathematics interest, self-efficacy, and achievement among a nationally representative sample of over 5000 adolescents hailing from Shanghai, China. The results of the study revealed that mathematics teachers’ use of cognitive activation strategies in their lessons – asking students to apply what they have learned to new contexts, encouraging students to reflect on problems, helping students to learn from mistakes they have made, presenting problems with no immediately obvious method of solution, giving problems with multiple solutions, and asking students to use their own procedures for solving complex problems – was significantly associated with higher mathematics interest, self-efficacy, and achievement. The findings of the study shed light on the key roles that mathematics teachers’ use of cognitive activation strategies play in enhancing students’ mathematics interest, self-efficacy, and achievement. The results of the study also highlight the need to create a mathematics teaching force which is capable of effectively and efficiently employing varied cognitive activation strategies in their lessons. However, further research is warranted to investigate the validity and efficacy of these strategies in other cultures.

Keywords: mathematics achievement, mathematics self-efficacy, cognitive activation, mathematics lessons, mathematics interest

**Introduction:** The hippocampus, a brain region involved in learning and memory, is thought to play an important role in the functions of the hypothalamic–pituitary–adrenal axis (Olton et al., 1979). It is well established that the hippocampus has an important role in memory function (Squire, 1985). The dentate gyrus, CA1 and CA3 regions of the hippocampus appear to be critically involved in cognitive function. In aged rats, loss of synapses in the dentate gyrus was related to memory deficits (Geinisman et al., 1986), as is loss of neurons in the CA1 and CA3 regions (Meaney et al., 1988). In younger animals, colchicine and kainic acid-induced lesions of granule cells and CA3–CA4 regions, respectively, impair formation of place learning (Whishaw, 1987). All the above data indicate the importance of hippocampus in memory. The hippocampus is critically involved in mediating spatial learning (Morris et al., 1982).

**Methods:** We investigated the effects of long-term adrenalectomy, 5 months after surgery, on spatial memory tasks. Moreover, the effect on locomotion and rearing was also investigated. The fact that adrenalectomy produces impairment on spatial learning which led us to determine the loss of hippocampal neurons. In this respect, we investigated the effect of long-term adrenalectomy on hippocampal neuronal survival. The neuroendocrine and the immune systems are interconnected. Monoclonal antibodies against major histocompatibility complex (MHC) class I, class II, CD4, CD8, pan T cells, and macrophages were used for immunostaining brains from adrenalectomized (ADX) and sham-operated rats to investigate the potential involvement of the immune/inflammatory mechanisms in the neurodegeneration of hippocampus after ADX. Using various antibodies to the amyloid β precursor protein (APP) associated with Alzheimer’s disease, we investigated changes in the distribution of APP in the hippocampus and neocortex of adrenalectomized (ADX) rats.

**Results:** Our results showed that the performance of bilateral adrenalectomised rats in the Morris water maze was significantly retarded when compared to sham-operated rats (Islam et al., 1995). Oitzl and De Kloet (1992) found that adrenalectomy impaired performance of rats in the maze 3 days after the surgery. Conrad and Roy (1993) attributed the learning deficits in long-term adrenalectomised rats to the dentate gyrus damage, rather than to absence of corticosterone, since the adrenalectomised
rats were still impaired even when corticosteroids were administered exogenously during training. In the retention test, in contrast to the observations of Conrad and Roy (1993), we observed that the ADX rats spent significantly shorter time in the platform circle compared to the sham and the naive controls (Islam et al., 1995). This further strengthens our finding that the ADX rats were more significantly impaired in learning the Morris water maze task compared to the sham and the naive control rats. Our findings of the open-field test showed no differences in number of locomotion counts between ADX and sham-operated rats. However, rearing was significantly decreased in the ADX compared to the sham and the naive control rats. Since rearing represents more explorative behavior, it can be suggested that rearing is probably more affected by adrenalectomy (Islam et al., 1995). Our results showed that the complete absence of adrenocortical hormones after long-term adrenalectomy leads to granular and pyramidal neuron degeneration (Adem et al., 1994). Our results demonstrate upregulation of MHC class II, CD4 antigens, and activated microglial marker-ED1 expression selectively in the hippocampus after ADX. The absence of CD5 reactivity precludes that these activated cells were T lymphocytes (Islam et al., 1997). The activated microglial cells may either be instrumental in the hippocampal neuronal loss or activated secondarily to the neuronal degeneration after long-term adrenalectomy (Islam et al., 1997). Our results showed that 5 months ADX rats showed striking APP reactivity in the CA1–CA4 fields and in the surviving cells in the dentate gyrus. These findings suggest the enhanced APP reactivity in hippocampal neurons after long-term hormone deprivation would be another factor, which may influence the expression of APP in brain (Islam et al., 1998).

**Conclusion**: In conclusion, our findings demonstrate that long-term adrenalectomy results in impairment of spatial learning and a decrease of explorative behaviour in ADX rats (Islam et al., 1995).

**Keywords**: microglia, neurons, spatial behavior, rearing, bilateral adrenalectomy, amyloid precursor protein, hippocampus

**REFERENCES**


Does progress monitoring increase student achievement? Curriculum-based measurement in mathematics

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In today’s educational climate, priority must be given to teaching students how to learn, more than what to learn, especially with the increasing number of students with special needs. Self-regulation and metacognitive strategies, such as goal setting, monitoring progress, and adapting, are vital to teaching students how to learn and become lifelong learners. A meta-analytic study was conducted addressing curriculum-based measurement, a form of progress monitoring, in mathematics (CBM-M) as an intervention. For purposes of the meta-analysis, an intervention was defined as using CBM-M at least bi-weekly for a minimum of 12 weeks, and data were used to inform instructional decisions. Studies included in the meta-analysis had to be quantitative, conducted in the United States, included only grades K-12, focused on mathematics, utilized CBM for at least 12 weeks, applied CBM at least bi-weekly, included pre–post data, and contained control, contrast, and/or comparison groups. The three research questions discussed include (a) what are the effects of implementing CBM-M as an intervention when digits correct are assessed for computation and concepts and applications? (b) what are the effects of CBM-M as an intervention when problems correct are assessed for computation and concepts and applications? and (c) what are the effects on overall mathematics achievement when CBM-M as an intervention is implemented? Detailed feedback incorporated information beyond the score, such as concepts mastered and instructional recommendations. Digits correct refer to grading an answer to a mathematical problem based on the accuracy of numerical place value. For example, if a student’s response was “1684,” but the correct answer was “1774,” the student would get a score of 2/4 correct for this particular problem because the “1” and “4” are correct and in the right place values. Problems correct assess the answer as a whole. Using the example above, the student would receive a score of 0/1 for the response since the number, as a whole, was incorrect. Specific outcomes for students in grades K-12, including those in general education and special education, when detailed feedback was utilized and when detailed feedback was not incorporated, were also examined. Upon completion of the meta-analysis, results indicated that when digits correct were assessed for computation, all students had a higher statistically significant effect when detailed feedback was utilized. More specifically, students in general education experienced higher effects when detailed feedback was
used, whereas students in special education benefited from CBM with or without detailed feedback. No studies were found for addressing concepts and applications with digits correct. When addressing problems correct for computation, all students had the most statistically significant benefit when detailed feedback was incorporated, yet students in general education had the most benefit. Much more data are needed in the area of problems correct for concepts and applications. From the data gathered, small non-statistically significant effects were found for all students without the inclusion of detailed feedback; yet, a negative non-statistically significant effect was found for students in special education. Not enough data were found to assess the use of detailed feedback. In terms of overall mathematical achievement, data were only found for the inclusion of detailed feedback. Results indicated that students in general education achieve small statistically significant effects, whereas students in special education did not show an effect at all. Overall, using detailed feedback produced higher statistically significant effects for students in both general and special education; however, the effects were higher for students in general education. Perhaps a lack of metacognitive and self-regulatory strategies is at the root of why students in special education did not benefit as greatly as students in general education from detailed feedback. Most research has been conducted in the area of computation for grades 3–6. Much more research is needed in the areas of concepts and applications, overall mathematical achievement, and at the secondary grade levels. Furthermore, a deeper look into why detailed feedback was not as effective for students with special needs, as for those in general education, needs to be examined, and could point to differences in information processing between the two groups.

**Keywords:** mathematics, self-regulation, metacognition, special education, progress monitoring, general education, curriculum-based measurement

Neurofeedback and biofeedback: applications in neuroscience

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Our emerging insights into neuroplasticity continue to open new therapeutic frontiers in neuromodulation and self regulation. Psychophysiological interventions, such as neurotherapy and biofeedback, have a history spanning decades, but their pivotal role in treating ADHD, anxiety, learning disabilities, depression, and a spectrum of other disorders has become increasingly recognized through peer-reviewed research. Self regulation and feedback therapies provide the means to shape an individual’s neurological and physiological responses. This webinar introduces neurofeedback and biofeedback concepts and demonstrates how the therapy process unfolds utilizing a case review of a patient treated with these modalities. Attendees will be able to experience an example of a recorded training session that demonstrates how the patient is able to receive and respond to physiological feedback. The presentation will also provide an overview of current research for common disorders, equipment used for therapy and the certification processes available both internationally and in the United States. Learning goals: the participant will be able to summarize the basic mechanics of a feedback session. Provide an example of how self regulation therapies have been used in the treatment. Outline empirical support for psychophysiological interventions.

Keywords: biofeedback interventions, neurofeedback training, neurotherapy, EEG biofeedback, neurofeedback for psychiatric disorders

REFERENCES


What are skills, and what does disrupt skillful performance? The theoretical background of a portable dynamic EEG study on choking effect

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An important aspect of education that can be studied with the help of neuroscientific methodologies is skill acquisition. What are skills, how do we learn them, and what psychological factors disrupt them? The study we are conducting at the Interdisciplinary Cog Sci Lab of UAE University addresses these issues by complementing behavioral experimentation with the data collected through a portable dynamic wireless EEG system. Our approach targets skill disruption (aka “choking effect”) as a way into more fundamental questions concerning the acquisition and the very nature of skill: is skillful expertise acquired through a process of automatization of sensorimotor routines? Is skill disrupted when the automatic flow of pre-reflective activity is interrupted by explicit monitoring and conscious control? In order to answer these questions, our study combines behavioral and EEG paradigms. Some influential studies in sport psychology (e.g., Beilock and Carr, 2001) suggest that choking affects expert athletes when they perform in pressure-field environments (e.g., during tournaments) because they tend to compulsively monitor the component processes of their own actions: the fluidity of the automatized motor routines (as in a golf putting task) is not disrupted by cognitive overload or distraction, but by the explicitly analysis of one’s own movements. Today, this model is under attack from multiple directions [reviewed in Cappuccio (2015), Cappuccio (2016), and Christensen et al. (2016)]: some converging lines of experimental research and theoretical investigation argue that, even if conscious control is not always necessary to expert performance, in many cases, it offers a great help. In spite of their apparent opposition, probably these approaches can be integrated, as each of them can help highlight at least some of the factors involved in the disruption of skillful performance. Portable EEG technology could allow us to measure when exactly, and to what extent, these factors intervene, suggesting when it is preferable to rely on one model of choking or the other. We will build on an experimental paradigm that has already been effectively used to identify the EEG markers of certain specific brain activities [de-synchronization of the Mu rhythms in the alpha-beta range, associated with the recruitment of the motor system in the preparation to cognitive tasks involving spatial reasoning, see Babiloni et al. (2008)] that consistently predict success during the early stages of skillful activity (golf putting again). In order to complement, and possibly critically discuss, the validity of the theory by Beilock and Carr (2001), we are
studying how the effect found by Babiloni et al. (2011) is modulated by experimental conditions that interfere with automatic routines (self-monitoring instructions) and/or reduce the effectiveness of the skillful expertise of the subjects (unfamiliar tools).

**Keywords**: EEG, skill acquisition, sport psychology, skill, choking under pressure

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The investigation of EEG specificity in epileptic children during AED therapy

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**Background:** Antiepileptic drug (AED) therapy in epileptic children can be optimized via an anticipation of AED efficacy during early stages of therapy. We hypothesize that the comprehensive EEG evaluation can determine AED efficacy in epileptic children. Thus, this study aimed to investigate the alteration of characteristics of interictal EEG during AED therapy.

**Methods:** Forty-three children aged 3–9 years were investigated. EEGs were recorded three times: prior to Valproic Acid-Depakine (Dep) monotherapy and twice under Dep therapy (at 3 and 6/8 months). Baseline EEG was analyzed for quantitative characteristics of interictal EEG such as absolute values of the power (AVP) spectra and EEG topography/brain mapping. The study involved epileptiform EEG and clinical condition assessments.

**Results:** Dep decreased AVP spectra in a low-frequency range, suppressed spontaneous epileptic discharge, and spike-wave complex 3/s. Dep partially decreased spikes–polyspikes, sharp waves, and generalized paroxysmal bursts during functional trials. Dep did not diminish rhythmic monomorphic theta-waves (RMT) of tempo-parietal localization observed by Brain Mapping. The presence of RMT correlated with the reoccurrence of seizures if Dep was withdrawn.

**Conclusion:** The findings of this study suggest that the presence of RMT with tempo-parietal localization on the interictal EEG can anticipate reoccurrence of seizures if Dep dose will be reduced or withdrawn. The efficacy of AED-therapy can be revealed via reduction of low-frequency waves and suppression of epileptiform EEG elements parallel to clinical improvement. Thus, optimal treatment strategies can be tailored based on the evaluation of background EEG characteristics using spectral analysis, EEG mapping, and the quantitative EEG approach.

**Keywords:** brain, epilepsy, antiepileptic drugs, qEEG, EEG power spectra
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