**Abstract #1**

**Reduced dependency of interneuronal correlation on tuning similarity accounts for behavioral suppression**

The spiking responses of neurons in sensory cortex are modulated by the properties of external stimuli. Indeed individual neurons can exhibit exquisite sensitivity to stimulus features. However, this single-neuron sensitivity is of limited utility for stimulus encoding for two reasons. One is that neuronal responses are modulated by multiple stimulus dimensions, so that identical responses can be associated with very different stimuli. Another reason is that single-neuron responses can be quite variable, so that the response to the same stimulus can differ from one presentation to the next.

Some of this variability can be reduced by combining the responses of multiple neurons. Indeed if the variability is independent across neurons, it can be eliminated by simply averaging the responses of many neurons. In this case the available information about the stimulus theoretically increases with neuronal population size. However, in reality neuronal noise is usually correlated across nearby neurons, and according to many models such *noise correlations* limit the fidelity of a population code. Thus current theories predict that stimulus information will either increase or saturate as the size of the neuronal pool activated by the stimulus increases.

Here we report a result that is contrary to both of these predictions. We recorded from neurons in area MT of macaque monkeys trained to report the perceived direction of a moving stimulus. Because MT contains a retinotopic representation of visual space, we manipulated the number of neurons contributing to the stimulus representation by changing the size of the stimulus. We found that as stimulus size (and hence the neuronal pool size) increased, the stimulus representation deteriorated drastically, as did the behavioral performance of the subjects.

The reason for this counterintuitive result is a previously unknown connection between stimulus sensitivity and noise correlations. Neurons that exhibited high sensitivity also exhibited detrimental noise correlations, so that as a population they signaled motion direction poorly. In contrast, neurons with more advantageous noise correlations had low stimulus sensitivity. This pattern of results could be due to inhibitory mechanisms, such as those commonly invoked in normalization models, which regulate both stimulus sensitivity and noise correlations.

**Abstract #2**

## Brain and behavioural correlates of dance versus music training

**Introduction:**
Individuals with specialized training provide an opportunity to investigate human brain plasticity and the interaction between the brain and behaviour. Specifically, those with artistic auditory-motor training, such as dancers and musicians, allow the study of sensorimotor integration and the fusion of sensorimotor expertise with artistic performance. Although dance and music training have similarities, such as the importance of sensorimotor integration, their artistic components and the easily quantifiable nature of the training process, they also possess several differences. Music training generally focuses on producing sound using fine motor skills, while dance training commonly focuses on following sound using gross motor skills. This study aims to examine the specificity of long-term dance versus music training on gray matter structure and behaviour.

**Methods:**
We used magnetic resonance imaging to measure cortical thickness (CT) and cortical surface area (SA) in 20 expert dancers, 19 expert musicians and 20 untrained controls. Participants were also tested on a battery of music- and dance-related tasks, including a dance video game. Statistical analyses were performed across the whole brain to test for group differences in CT and SA, as well as regions where CT or SA are correlated with task performance.

**Results:**
Both dancers and musicians showed greater cortical thickness than controls in the superior temporal gyrus. Cortical thickness in the superior temporal gyrus was correlated with performance on both dance- and music-related tasks. Additional cortical thickness results were found in somatosensory and motor regions. Surface area results were found in occipital and frontal regions.

**Conclusions:**
These results suggest that dance and music training similarly affect brain regions associated with auditory processing, specifically the STG. This work advances our understanding of the specificity of the neural correlates of dance and music training, and may have potential applications in therapies for motor disorders.

**Abstract #3**

Prior imaging studies have shown that the right posterior superior temporal cortex is activated by visual motion stimuli in deaf persons. Based on research in deaf cats, this cross-modal reorganization of auditory cortex would be predicted to support compensatory visual enhancements in deaf humans. However, the nature of these behavioural changes, and the mechanism of this plasticity, are not known. My research demonstrates that visual motion detection is enhanced after deafness, and that this ability is related to cortical thickness in the right posterior superior temporal cortex. This work draws a connection between cross-modal plasticity and compensatory behaviour after deafness, and indicates an anatomical correlate – cortical thickness – of this plasticity. These results will be discussed in context of a new theory for cross-modal reorganization after deafness, in which changes to the attentional system for sensory reorienting lead to increased visual reactivity in this population.

**Abstract #4**

## Optogenetic manipulation of theta rhythm reveals REM sleep-dependent cognitive processing

Rapid-eye-movement (REM) sleep is present in nearly all terrestrial mammals studied to date and has been positively correlated with memory formation. However, identifying a direct causal link between neural activity during REMs and memory has proven difficult due to a sporadic pattern of occurrence in addition to a spectrum of critical caveats associated with REMs deprivation techniques. To overcome these issues we genetically targeted inhibitory archaerhodopsin (ArchT) to GABAergic neurons of the medial septum (MS), a brain region required for *in vivo* generation of the theta rhythm, a prevalent ~7 Hz oscillation present during active wakefulness and REM sleep that is linked to cognitive processing. We found that green light pulses reliably hyperpolarized ArchT-expressing cells by ~ 40 mV, preventing spiking in transfected neurons completely, in the MS in brain slices *in vitro*. Using a combination of optogenetic and electrophysiological (MS unit recording and dorsal hippocampal CA1 field potential and unit recording) techniques in freely-behaving mice, we further found that green light delivered to the MS could completely and reversibly silence putative MS GABAergic neurons with <1 s temporal resolution. Silencing GABAergic neurons during REMs resulted in a significant (> 60%) and reversible attenuation of the theta rhythm amplitude recorded in the dorsal CA1 region of the hippocampus without disturbing the ongoing REMs episode. To determine whether MS GABAergic activity during REMs is involved in memory formation, we tested mice in a novel object place recognition test as well as a fear conditioning task. During the four hour period immediately following the learning phase of each test, MS GABAergic neuronal activity was silenced selectively during REMs. When tested the following day, novel object place recognition and fear-conditioned contextual memory were both found to be significantly impaired relative to controls. Collectively, our results identify MS GABAergic neurons as one of the major generators of the hippocampal theta rhythm, and, provide a direct causal link between MS GABAergic neuronal activity during REMs and memory formation.

**Abstract #5**

**A model of epilepsy based on optogenetic kindling**

How healthy neuronal circuits undergo epileptogenesis is not well understood. To facilitate the study of circuit changes associated with epileptogenesis, we developed a novel optogenetic animal model of epilepsy. Based on the classical kindling paradigm, we hypothesized that seizures can be elicited solely by repeated overactivation of a subset of neurons. To test this, we targeted Channelrhodopsin-2 (ChR2) to primary motor cortex (M1) of male C57BL/6J mice by stereotactic delivery of AAV-CaMKIIa-hChR2-E123T/T159C-p2A-EYFP. After 21 days of recovery, we kindled M1 of awake behaving animals with a 445-nm laser while recording EEG and video. To test if kindled animals retained the potential for seizures in the long term, stimulations were paused for 36 days, after which kindling was resumed.

We found that seizures gradually emerged after 15.3 ± 2.1 sessions in 6 out of 6 animals. These seizures were defined as periods longer than 3 seconds where EEG power exceeded noise levels by two standard deviations. We quantified seizure duration by EEG, and severity by a modified Racine scale. We found that the duration ($r=0.52$, $p<0.001$, $n=4$) and severity ($r=0.59$, $p<0.001$, $n = 4$) of seizures increased with session. Seizure onset threshold was also reduced ($r=-0.59$, $p<0.001$, $n = 4$), and the average number of seizures increased over session ($r=0.48$, $p<0.001$, $n = 6$). In rekindled animals, we found that seizures had a higher Racine score ($p< 0.05$, $n=5$) and were longer lasting ($p<0.01$, $n =4$). Rekindled animals also had a lower seizure threshold ($p < 0.01$, $n =4$), and the number of sessions until first seizure was significantly reduced ($p< 0.05$, $n=4$). Preliminary histology indicated that our optogenetic approach caused no appreciable glial activation, nor any major injury.

In summary, we found that repeated optogenetic stimulation of awake behaving animals eventually elicited seizures in the absence of gross brain damage, and that animals retained an elevated seizure susceptibility for weeks. As our model allows for the identification of directly activated cells, it enables the investigation of the role of specific cell populations in epileptogenesis.

**Abstract #6**

## Synaptic and locomotor defects in a zebrafish genetic model of Amyotrophic lateral sclerosis

Amyotrophic lateral sclerosis (ALS) is a devastating neurodegenerative disease characterized by the progressive dysfunction and then death of upper and lower motor neurons in the spinal cord and cerebral cortex. About 4% of familial ALS cases can be attributed to point mutations in *TARDBP* (encoding the TDP-43 protein) and interestingly, the majority of sporadic ALS cases, which account 90% of all ALS patients, display an abnormal accumulation of misfolded TDP-43 in the cytoplasm. To study the pathophysiological role of TDP-43, we have obtained (by TILLING mutagenesis) a mutant zebrafish line containing a premature stop codon (Y220X, denoted '-') in the *tardbp* gene. As a result of the genome duplication that occurs in zebrafish, Homozygous *tardbp*$^{-/-}$ zebrafish do not produce tdp-43 protein yet still develop normally because they are compensated by an alternative splicing of the *tardbp-like* ortholog. Therefore, in order to obtain a true reduction of *tardbp* expression, we injected homozygous *tardbp*$^{-/-}$ fish with an antisense morpholino (MO) targeting the *tardbp-like* gene, ultimately creating a double mutant. These *tardbp*$^{-/-}$ mutants injected with the MO displayed impaired locomotor performance, characterized by a reduction in swim distance, swim duration and maximum swim velocity when compared to heterozygous and wild type zebrafish larvae. Additionally, protein extraction and Western Blots were performed and confirmed the reduced expression of *tardbp* and *tardbp-like* protein products in morphant *tardbp*$^{-/-}$ larvae. In current experiments, we are taking a step further in order to characterize the aberrant synapses in these morphant larvae. We are recording glutamatergic miniature excitatory post-synaptic currents in primary motoneurons in order to characterize changes in synaptic inputs following tdp-43 depletion. Understanding both the behaviours and synaptic changes will aid in our understanding of the pathological mechanisms that ultimately result in motor neuron death in TDP-43-related ALS cases. In particular, at pre-clinical stages of the disease, where very little is known about the early pathophysiological disturbances that occur in this disease. Additionally, this project may help eventually identify novel therapeutic targets to improve synaptic function in ALS patients, as well as among patients with other motoneuron diseases.

**Abstract #7**

**Fragile-X Related Protein 1: A Key Player in Synaptic and Memory Functions**

For hundreds of years researchers have tried to understand how memories are formed, where in the brain they are stored and whether we can alter their content, and if so how. When a memory is formed in the brain, information is processed and strengthened by producing specific proteins. However, the production of these proteins in the brain is highly controlled by other proteins, which are known as mRNA binding proteins. These proteins bind and regulate the translation of target mRNAs, which are recruited during memory formation, maintenance and storage. The goal of the project is to study the function of an mRNA binding protein known as the Fragile-X related protein 1 (FXR1P). Specifically, we are trying to understand how FXR1P affects memory functions in the brain by controlling the mRNA translation and in turn, the production of proteins that are required for the strengthening and maintenance of memories. What we have found is that if we remove the expression of FXR1P from an area which is important for learning and memory, known as the hippocampus, our FXR1P-lacking mice show enhanced long-term potentiation, enhanced memory storage, as well as enhanced production of GluA2 protein (an important molecule in memory strengthening and synaptic transmission). Through this project, we have discovered a novel memory pathway that can be modified by changing the expression of specific mRNA binding proteins such as FXR1P. Our future goal is to try and analyze this pathway further with the hope of developing therapeutic methods for the treatment of disorders characterized by deficits in learning and memory processes, as seen in Alzheimer's disease.