Chapter 1 : Frontiers Lecture: Probing Asteroids in Space | AMNH

Probing the Frontiers of Biblical Studies is a seventeen-chapter anthology on biblical studies. It has been crafted as an extended and respectful thank you note to one of the most insightful scholars of biblical studies, David J. A. Clines of Sheffield University in England.

This can be explored at various spatial scales, from individual neurons to macroscopic neuronal populations. The functional connections between brain regions are most often inferred from functional magnetic resonance imaging fMRI of the brain at rest. Functional MRI provides a non-invasive means to map brain function at millimeter spatial resolution. However the temporal resolution of fMRI, typically of the order of seconds, limits its ability to capture the full dynamics of neuronal processes. Scalp electroencephalography EEG can also be used to construct a functional connectome. Whilst it has limited spatial coverage and much poorer spatial resolution than fMRI, EEG can measure brain activity with the millisecond temporal resolution required to capture neuronal dynamics. It is also possible to acquire EEG and MRI simultaneously, potentially allowing a richer measure of brain connectivity by combining complementary measures. Combining information from EEG and fMRI is not a trivial exercise due to the different sensitivity, temporal and spatial scales of the measures for a recent review, see Jorge et al. Each channel of the EEG comprises a superposition of signals arising across a spatial scale of several centimeters, whilst the fMRI signal at each spatial voxel is sampled just once every few seconds. The EEG measure is electrical and therefore directly related to neuronal activity, whereas fMRI relies on a blood oxygenation level dependent BOLD contrast that is indirectly related to neuronal activity Ogawa et al. Thus, the sensitivity of each modality has different dependencies on underlying physiology and morphometry, and in some cases activity visible on one modality may not be seen on the other Nunez and Silberstein, The complementary information that each modality can provide at a whole-brain connectome level has only recently begun to be explored. Nodes of the connectome were determined from an anatomical parcellation of T1-weighted structural MRI 68 cortical and 14 subcortical regions. Due to the poor spatial resolution of EEG, estimating average time series for each region was necessarily more complex for EEG than the simple voxel averaging approach required for fMRI. The EEG was first filtered into five frequency bands and source localization using beam forming was undertaken for each band. The band-limited power envelope of the EEG was then used to estimate a time series for each cortical gray matter region. For fMRI and for each frequency band of the EEG, a functional connectome was estimated by deriving covariance matrices effectively a partial correlation analysis. Functional connectomes were calculated for about Stationarity of functional connectivity was assumed, although this is not a fundamental limitation of the approach; for example the authors note that sliding window correlation could be employed to examine time varying functional connectivity. The functional connectomes derived by Deligianni et al. For example the cortical EEG connectomes exhibit a bias toward intra-hemispheric connections, whereas the fMRI connectome tends to exhibit a more uniform mix of inter and intra-hemispheric connections. It also suggests that, at least at the spatial resolution of the atlas-based parcellation used, the band-limited power of the EEG may capture more information on the dynamics of cortical brain activity than fMRI. This is a particularly interesting observation, given that atlas-based parcellation is a common processing strategy for fMRI functional connectivity. One should bear in mind though that this is a relative comparison: Whilst simultaneous EEG and fMRI acquisition is now a mature technology mix, EEG quality can potentially be improved further with the addition of motion artifact detection sensors e. This would be advisable in future studies of functional connectivity with EEG-fMRI, given recent demonstration of spurious correlations driven by in-scanner movement Fellner et al. Nevertheless, the greatest potential for future advancement in EEG-fMRI is in methods to make the most of the information captured by each modality. This is highlighted by the work of Deligianni et al. Author Contributions The author confirms being the sole contributor of this work and approved it for publication. Conflict of Interest Statement The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest. The reviewer AN and the handling Editor declared their shared affiliation, and the

handling Editor states that the process nevertheless met the standards of a fair and objective review.

Chapter 2 : Probing the Molecular and Genetic Frontiers of Drug Abuse Research | NIDA Archives

The field of particle physics is in a peculiar state. The standard model of particle theory successfully describes every fundamental particle and force observed in laboratories, yet fails to explain properties of the universe such as the existence of dark matter, the amount of dark energy, and the preponderance of matter over antimatter.

Our findings support the hypothesis that the phonological encoding in speech production for Chinese language may approximately start from ms and end around ms post target onset, a little earlier than that from ms to ms for Indo-European languages. Introduction Spoken word production involves the coordination of several consecutive processes, such as conceptual preparation, lexical retrieval, phonological encoding, phonetic encoding and articulation. According to an influential language production model Levelt, , a critical phase in this process is phonological encoding during which the phonological form of the target needs to be prepared to guide the subsequent articulatory movement syllabic encoding. The processes of phonological preparation have been referred to as phonological encoding Wong et al. Based on a meta-analysis, Indefrey and Levelt estimated that the time course of phonological encoding starts from ms and ends around â€" ms during the process of word production Indefrey and Levelt, , and this estimate has been widely supported by many studies of Indo-European languages Salmelin et al. Nevertheless, it is not self-evident that the above findings from Indo-European languages can be generalized across all world languages. The proximate units are phonemic segments and metrical frames for Dutch and English Levelt, , atonal phonological syllables and tonal frames for Mandarin Chinese Chen et al. Indeed, studies on Mandarin and Cantonese spoken word production failed to find convergent results with studies on Indo-European languages concerning the time course of phonological encoding in word production Qu et al. More positive ERPs signals evoked by phonologically related words were observed from ms to ms post target presentation, indicating that the time window ms to ms is the critical period for phonological encoding for Mandarin Chinese. More recently, another study with similar picture naming paradigm was conducted by Wang et al. A significant phonological-related ERP effect was found in the time window of â€" ms after picture onset. Similarly, in a color adjective-noun picture naming task, Qu et al. Taken collectively, these findings provide empirical evidences for language-specific aspects in the process of phonological encoding. Most of recent studies on speech production are conducted by way of magnetoencephalography MEG and electroencephalography EEG for their high temporal resolution, but these techniques might not be the optimal tools to systematically investigate language function at each particular region or time point. Nevertheless, transcranial magnetic stimulation TMS might be a valuable tool to transiently disrupt or even enhance language function during task performance. More importantly, it can be used by changing its stimulation pulse onset and by analyzing stimulation-related impairment of language function at each particular time point and region Indefrey, ; Krieger-Redwood and Jefferies, ; Krieg et al. In this sense, some TMS-related studies have already been conducted to investigate the influence of stimulation onset on picture naming task Schuhmann et al. For example, Schuhmann et al. A follow-up study of Schuhmann et al. Furthermore, in a study performed by Wheat et al. Therefore, TMS is an effective way in investigating the time course of word production. However, most previous studies with TMS technique mainly focused on the alphabetic languages such as English and Dutch Schuhmann et al. As mentioned above, phonemic segments and phonological syllables play a different role in the process of phonological encoding between Mandarin Chinese and alphabetic languages like English and Dutch. To make a comparison between Chinese and alphabetic languages such as Dutch, in the present study, we used Schuhmann et al. In the light of prior EEG and MEG findings of cross-linguistic difference in the latency of phonological encoding, we propose a hypothesis that the phonological encoding in word production for Chinese language may approximately start from ms and end around ms post target onset, a little earlier than that from ms to ms for Indo-European languages. All participants were right handed, had normal or corrected-to-normal vision and had no history of neurological or psychiatric disorders. Standard exclusion criteria for TMS were applied: All participants gave written informed consent before the experiment and received monetary rewards after the experiment. The TMS session was performed according to the

published safety guideline. All participants tolerated the TMS procedure well and did not report any adverse effects. Stimulus Materials Twenty simple white-on-black line drawings corresponding to double-word Chinese nouns as target pictures were selected from a data base of standardized pictures for picture naming tasks in Mandarin production Qingfang and Yufang, All target pictures were of moderate word frequency and familiarity as determined by studies of Qingfang and Yufang on picture naming latency during Chinese language production. Experimental Procedures The main experiment compared the effect of real vs. We applied triple-pulse real TMS and triple-pulse sham TMS in two separate sessions on two separate days respectively, during the execution of behaviorally controlled picture naming task in Chinese. The sequence of stimulation type was counterbalanced across participants. The study design enabled us to test for stimulation type and time effects of a controlled neutral activity disruption on Chinese picture naming latencies. A new trial began with a fixation cross presented between ms and ms. Thereafter, a target picture was presented for ms, followed by a blank screen for ms. Participants were instructed to name the presented picture as quickly as possible. Verbal responses were recorded by using a microphone placed in front of each participant. After a jittered delay between 6 s and 8 s, the next trial began see Figure 1. During the presentation of picture, triple pulse transcranial magnetic stimulation TMS stimulation was applied at one of the five time windows in a random way. Participants were instructed to name the presented picture as quickly as possible using a microphone placed in front of each participant. After a jittered delay between 6 s and 8 s, the next trial began. In order to exclude unspecific TMS effects, a control experiment was performed in another group of subjects. A specific figure-of-eight placebo coil MC-P-B70 was also employed in order to reproduce the same acoustic stimulation as the active coil while not inducing the magnetic field sham stimulation. The coils were manually held tangentially to the skull with the coil handle oriented perpendicular to the opercular part of the inferior frontal gyrus using the online visualization function of the BrainSight frameless stereotaxy system BrainSight Frameless, Rogue Research, Montreal, QC, Canada. The maximum output of the coil and stimulator combination was appropriately 0. The mean stimulation intensity of the tpTMS was about All the participants tolerated the tpTMS well and did not ask to stop the experiment nor did they pull their head away from the coil during the stimulation. The stimulation sites were determined on the basis of study by Schuhmann et al. The location of the target stimulation site was centered on the following MNI coordinates: For the TMS stimulation over the Vertex control experiment , this was localized as a midpoint between the inion and the nasion and equidistant from the left and right ear. Brainsight was used to track the position of the TMS coil throughout the stimulation period, ensuring that it remained on the target location. Coronal, axial, sagittal views of the stimulated site left inferior frontal gyrus, Montreal Neurological Institute MNI coordinates: The time interval between the two TMS sessions was 1 week to make sure that there were no carryover effects between the two sessions. Before starting the main experiment, participants were instructed to practice a training session to be familiar with the stimuli and to name the stimuli repeatedly as to reach a stable performance level in naming latency. Each experimental session consisted of trials, divided into four blocks of 30 trials each. Event-related tpTMS was applied at five different points in time following picture presentation onset, namely at: The presentation of the pictures and TMS time window conditions were applied randomly across trials within each session. There were mainly two reasons for the spacing of time windows. Lemma selection should begin between ms and ms post picture onset and be over at some moment between ms and ms post picture onset. Then phonological code retrieval may begin between ms and ms after picture onset. Syllabification takes place from ms to ms post picture onset. Finally, phonetic encoding may begin between ms and ms followed by articulation at about ms. Response Time Measures Verbal responses were recorded by using a microphone placed in front of each participant. The latency of the verbal responses was measured using the speech wave envelopes with digital audio editing software cooledit v2. Acoustic information was digitized at an 8-bit resolution with a sampling rate of 22 kHz. An amplitude filter was used to reduce the noise before the determination of the speech onset see Figure 3. Verbal response time analyses. Naming onset was defined as the first detectable amplitude in the speech wave envelop. The accuracy of verbal responses was checked offline by listening to audio recordings. One participant made a large number of errors due to discomfort of strong contractions of face muscles and therefore was excluded from the analysis. Statistical

Analysis RTs and correct response rates accuracy were measured. If necessary, sham TMS and real TMS session were further compared using post hoc t-tests, Bonferroni corrected for multiple comparisons. The mean amount of errors during the real TMS experiment ranged from 0. During the sham TMS experiment, the mean amount of errors was comparable, ranging from 0. The mean reaction times RTs of the five time windows in real and sham stimulation conditions. To determine the source of this 2-way interaction, paired t-test, Bonferroni corrected for multiple comparisons, were conducted to compare the respective five time points of stimulation between real and sham conditions. The results showed that RTs were significantly prolonged in the time window of ms, ms and ms compared to the other two time windows of ms and ms between real and sham condition real: To assess the difference between real and sham stimulation at five time windows, we calculated the TMS cost across time window. Meanwhile, separate one-factorial analyses of real and sham TMS were conducted respectively to compare the five different time windows under each stimulation type condition. And results showed that RT rapidly increased at ms compared to the first time window at ms. The mean RTs of the five time windows in real and sham stimulation conditions respectively. Vertex group as between-subject factor. A subsequent two-sample T test was applied to compare the TMS cost at five time windows between two groups. No between-groups effect was found. One explanation for the discrepancy between alphabetic and non-alphabetic languages invokes the cross-linguistic differences on the process of phonological encoding. For instance, as a non-alphabetic language, Chinese maps each graphical character directly into one syllable using orthography-to-phonology transformation. Whereas, alphabetic languages like German and English segment each word into letters and then translate into a phonetic sequence following the grapheme-to-phoneme conversion rules Tan et al. This model has been largely supported by a large amount of studies on alphabetic language such as English and Dutch Meyer, ; Schriefers et al. Nevertheless, studies on Mandarin and Cantonese spoken word production failed to find supporting evidence at segment level Chen et al. By the same token, more recently, Roelofs postulated the form network for Mandarin Chinese the following four levels: If this is the case, then the phonological encoding for Mandarin Chinese would involve an extra step compared with that for Indo-European languages Roelofs, Therefore, with similar naming latencies of ms in picture naming task between alphabetic and non-alphabetic languages, it is reasonable that the time course of phonological encoding for Mandarin Chinese is between ms and ms, a little earlier than that for alphabetic languages. However, there is no significant effect of TMS stimulation between sham and real stimulation at ms after picture presentation. It may be due to the fact that the mean RTs for speech production is around ms, so delivering tpTMS at ms may inevitably interfere with the process of speech production, which may result in an increase in RTs for real and sham stimulation respectively. Thus, future study should exclude those disturbances from investigation. One limitation of the current study is that we used different group of subjects in the control experiment with smaller sample size of subjects.

Chapter 3 : Probing the Viromic Frontiers

Although Broca's area is widely recognized to play an important role in speech production, neuroscientists still debate on its timing recruitment across different languages.

 This article has been cited by other articles in PMC. Recent HTS was used to identify and discover a previously undescribed member of the family Flaviviridae that has genomic features characteristic of both hepaciviruses and pegiviruses. This virus, designated human hepegivirus-1 HHpgV-1 , may represent a previously undescribed new genus in the Flaviviridae family with implications for public health and blood supply safety. Detecting uncharacterized viruses such as HHpgV-1 in clinical samples requires an unbiased screening method that is as sensitive as PCR, while simultaneously detecting multiple rare viral sequences. The virome-capture-sequencing platform for vertebrate viruses VirCapSeq-VERT uses positive-selection oligonucleotide capture to sensitively detect sequences from every known vertebrate virus, even in high-background specimens with low-abundance viruses. VirCapSeq-VERT can also detect uncharacterized viruses with sequence homology to known viruses, enabling a new paradigm for virus detection. COMMENTARY Modern molecular biology has accelerated the pace of virus discovery, allowing pathogen identification based on genome characterization to proceed much more rapidly than traditional virologic, microscopic, or serologic methods. In particular, high-throughput sequencing HTS has revolutionized the unbiased discovery of novel viruses, often in unexpected places that are highly relevant to human health. This is exemplified by a recent article by Kapoor and colleagues from W. Further analysis indicated that this virus combines features of hepaciviruses and pegiviruses, two distinct genera within the family Flaviviridae. This virus, named human hepegivirus-1 HHpgV-1 , may represent a new genus within the Flaviviridae and a potential human pathogen. Previous work from the Lipkin laboratory has enhanced our understanding of hepacivirus and pegivirus diversity in the wild. Hepatitis C virus HCV was long thought to be the sole member of the genus Hepacivirus, until the discovery of a novel canine hepacivirus 2 suggested that there may be greater hepacivirus diversity in nonhuman mammalian species. Since then, numerous hepaciviruses have been characterized in horses, bats, rodents, and nonhuman primates 3 , â€” 7. A similar host range diversity has been observed for pegiviruses 8. As HTS-based methods increase for viromics study applications, we also expect to discover additional novel members of Flaviviridae and develop a more comprehensive understanding of flavivirus biology. This suggests that like hepaciviruses, translation of the viral polyprotein occurs via a common internal initiation mechanism. HHpgV-1 also contained a distinguishing sequence in the pseudoknot domain that is highly conserved across the genus Hepacivirus. Thus, HHpgV-1 shares characteristics of both genera, suggesting either a common ancestor or recombination between two prototypic viruses. This raises the possibility that HHpgV-1 may cause chronic infections like other hepaciviruses and pegiviruses. It is currently unknown whether HHpgV-1 has the potential to cause a pathogenic infection, like HCV, or merely a silent, nonpathogenic infection similar to human pegivirus HpgV , which persists for years without causing disease in healthy people. HHpgV-1 may have substantial implications for public health, as Kapoor and colleagues detected the virus in posttransfusion samples, strongly suggesting transmission via transfused blood products. The blood-borne HCV was spread extensively by contaminated blood products prior to identification of the virus as the etiologic agent of the then-called non-A, non-B hepatitis and the subsequent development of tests to ensure the safety of the blood supply. While the consequences for human health are unknown, a more detailed assessment of HHpgV-1 prevalence in the population will start to yield answers. For this purpose, a precise, highly sensitive means of screening clinical specimens is essential. Ideally, this would require an unbiased method for detecting multiple HHpgV-1 variants, in addition to other related persistent viruses, with a sensitivity equal to or greater than the sensitivity of quantitative PCR. A decade ago, microarray-based technologies showed great promise for allowing the simultaneous detection of multiple viruses 9 , 10 ; however, low sensitivity has hindered these technologies from becoming standard for clinical diagnostics. While HTS can be used to perform unbiased

pathogen detection and discovery, this technology is still insufficiently sensitive for patient samples, in which viral sequences may be very rare Fig. Efforts to enrich pathogen sequences by depleting host nucleic acids has not sufficiently improved sensitivity to warrant using HTS as a standard diagnostic assay. Furthermore, the high cost and practical complexity of obtaining and analyzing data have delayed the implementation of HTS in clinical diagnostics, compared to relatively simpler, less-expensive virus-specific PCR-based methods. While PCR-based methods are highly sensitive, they cannot identify unknown pathogens and have been used only to confirm diagnosis of a suspected pathogen. Another recent article from the Lipkin laboratory by Briese et al. The virome-capture-sequencing platform for vertebrate viruses VirCapSeq-VERT represents a novel means of detecting every known vertebrate virus, even from limited clinical samples with high abundance of host background sequences.

Chapter 4 : CiteSeerX â€" Probing the Pareto frontier for basis pursuit solutions

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Chapter 5 : Probing the Frontiers of Biblical Studies : Dr J Harold Ellens :

Modern molecular technology, and particularly high-throughput sequencing (HTS), has revolutionized virus discovery and expanded the depth and breadth of the virome. Recent HTS was used to identify and discover a previously undescribed member of the family Flaviviridae that has genomic features.