Treacher Collins syndrome. A compound heterozygote consisting of 2 missense alleles in the TCOF1 gene was identified as a compelling pathogenic allele, necessitating further functional investigation. The study helped validate the use of the intuitive iobio tools in such analyses, strengthening the case for greater involvement of medical professionals in data analysis. DISCUSSION/SIGNIFICANCE OF IMPACT: The performed analyses demonstrated that the whole genome sequencing data for the family being studied was of a very high quality, although 1 gene demonstrated a local region of almost zero coverage. This ensured that study conclusions can be presented with confidence. A variant associated with Treacher Collins syndrome 1 in ClinVar was uncovered in the TCOF1 gene, however, given it's benign rating, this variant was not considered further. The most interesting candidate was a compound heterozygote, consisting of 2 missense mutations, also in the TCOF1 gene. These mutations occurred with allele frequencies of 22% and 8% in the general population, and additional molecular and functional studies are currently being pursued.

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HOME Cell 2.0. Extending i2b2 to support community health outcome monitoring and evaluation via web-accessible software

William G. Adams, Michael Mendis, Shiby Thomas, David Center and Sara Curran

OBJECTIVES/SPECIFIC AIMS: The primary objective of this effort is to develop and distribute an easy to use i2b2 component that is capable of evaluating diverse complex relationships for a wide variety of exposures and outcomes over time. In this manner we are able to leverage the unique design of the i2b2 database to support health services research, comparative effectiveness, and quality improvement using a single tool. Furthermore, our novel database redesign has the potential to provide user-friendly access to individual and group CHC data for CER. METHODS/STUDY POPULATION: For this project we used software experts, clinical informatics specialists, and the existing i2b2 open-source software to convert our legacy HOME Cell into a web-client version. The tool will be used to study health outcomes within a network of Boston based Community Health Centers and the largest safety-net hospital in New England, Boston Medical Center. RESULTS/ANTICIPATED RESULTS: The new web-client HOME Cell will allow i2b2 users to model virtually any exposure (including therapeutic interventions such as medications or tests) in i2b2 against any outcome accounting for complex temporal relationships and other factors. In addition we plan to use our new Community Health Center views to enhance our community engagement activities by allowing direct access to their data for our partners. DISCUSSION/SIGNIFICANCE OF IMPACT: Our project addresses multiple national priorities related to data sharing, clinical research informatics, and comparative effectiveness. The web-client version of the HOME Cell substantially improves our community's access to HOME Cell functionality and is a novel, sharable resource for use within the CTSA/NCATS community. Our approach provides a new way to perform large-scale collaborative research without the need to actually move patient-level data and has demonstrated that CER, health services research, and quality measurement can share a common framework. In addition, and as demonstrated in our earlier pilot work, the HOME Cell also has the potential to support large-scale multivariate analyses in a distributed manner that does not require sharing of patient-level data. We believe our approach has great promise for supporting the reuse of clinical data for rapid, transparent, health outcome assessments on a national scale. Our efforts support multiple strategic goals including: (1) support for building national clinical and translational research capacity by enhancing a broadly adopted informatics tool (i2b2); (2) enhanced consortium-wide collaborations by offering a tool that can be easily shared within the CTSA network to support multi-institutional collaboration; and (3) improving the health of our communities by offering a tool that has the potential to provide new insights into health care processes and outcomes that could drive innovation and improvement activities.

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Will the Veteran Affairs (VA) electronic medical records (EMR) database reveal a signal that angiotensin II inhibiting medications ameliorate depression?

David D. Maron, Marc Blackman, Richard Amdur, Thomas Mellman and Kathryn Sandberg

OBJECTIVES/SPECIFIC AIMS: Angiotensin type I receptor blockers (ARBs) and angiotensin-converting enzyme inhibitors (ACEIs) are frequently prescribed for hypertension and associated cardiovascular and renal complications. In animal models, these drugs also reduce anxiety and depression. OBJECTIVE—to determine if Veteran Affairs (VA) clinical pharmacy data indicate a protective effect of ARBs and/or ACEIs for major depression. METHODS/STUDY POPULATION: Pharmacy records from nationwide VA electronic medical records (EMR) were extracted for patients prescribed ARBs, ACEIs, α-blockers, β-blockers, calcium channel blockers, or diuretics (n = 4,081,359). Patients were excluded if: they had not received medications for 6 months with >70% coverage; were diagnosed with substance/alcohol abuse, dementia, psychosis, schizophrenia, or prescribed insulin. The study population was categorized as "ARB/ACEI" (A/A) or "Never ARB/ACEI" (NA/A). Using the Greedy Matching Algorithm, subjects were matched on a 1:1 ratio for sex and race over a 5 year age range resulting in 2 equal groups of n = 1,350,236 each. Subjects were older (M = 71.6, SD = 12) and mostly men (97%). RESULTS/ANTICIPATED RESULTS: In the A/A Versus NA/A, respectively, the incidence of anti-depressant use was greater during (9.9% vs. 8.9%) but was lower after (11.8% vs. 12.2%) the study period. PHQ-2 scores (Mean ± SD) were statistically lower, albeit similar, during (0.79 ± 1.56 vs. 0.85 ± 1.63) and after (1.00 ± 1.73 vs. 1.07 ± 1.79) the study period. DISCUSSION/SIGNIFICANCE OF IMPACT: These preliminary data suggest that inhibiting angiotensin II action does not provide a protective effect on major depression when compared with other classes of antihypertensive drugs. This study illustrates how "Big Data" may inform the design, or obviate the need, for large-scale randomized-controlled trials.

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Passive intracranial EEG-based localization of the central sulcus during sleep

Rafeed Alkawadri
Yale School of Medicine, Guilford, CT, USA

OBJECTIVES/SPECIFIC AIMS: To investigate the performance of a metric for passive localization of central sulcus. METHODS/STUDY POPULATION: We studied 7 patients with intractable epilepsy undergoing intra-cranial EEG (icEEG) monitoring at Yale, in whom central sulcus (CS) localization was obtained by standard methods. Our method takes advantage of inherent properties of the primary motor cortex (MC), which exhibits enhanced icEEG band-power and coherence across the CS. For each contact x we calculated the z-score of a composite power and synchrony value $\log_{10}(px)\,x;cx$, where px is sum of the root mean square of the icEEG in the high gamma band (80–115 Hz) for contact x over the 6–10 minutes of NREM sleep studied, and cx is the mean magnitude squared coherence in the same band using a 500-ms Hamming window between contact x and all other contacts. z-score values lower than threshold (th) were set to 0. Finally, we calculated a metric $m = z/d$, where d is the mean Euclidian distance of each contact from contacts with z scores greater than 0. The last step was implemented to emphasize local network activity. RESULTS/ANTICIPATED RESULTS: We report the results of a pilot study to test the performance of a new operator independent method for passive identification of CS with intractable epilepsy undergoing icEEG monitoring at Yale, in whom CS localization was obtained by standard methods. The sensori-motor (SM) cortex exhibited higher EEG-gamma power compared with non-SM cortex ($p < 0.0002$). There was no significant difference between the motor/premotor and sensory cortex ($p < 0.47$). CS was successfully localized in all patients with thresholds between 0.4 and 0.6. In 2 patients, knowledge of anatomy was needed to distinguish the MC from adjacent epileptic foci. The primary hand and leg motor areas exhibited the highest metric values consistently followed by the tongue motor area. Higher threshold values were very specific (94%) for the anterior bank of the CS but not sensitive. Intermediate threshold values achieved a reasonable trade-off (0.4: 89% specific and 70% sensitive). DISCUSSION/SIGNIFICANCE OF IMPACT: We present and successfully implement a rapid procedure for task-free and stimulation free localization of the central sulcus during sleep based on intrinsic electrophysiological properties of the primary motor strip which exhibits increased power and enhanced local connectivity. We successfully localized the central sulcus in all patients. When implementing appropriate thresholds, our proposed metric M is very specific for the anterior lip of the central sulcus which may make it ideal to identify this important anatomical landmark. Our method is sensitive for epileptogenic regions as well, therefore basic knowledge about central sulcus anatomy may be needed in cases where there is an epileptogenic lesion in the vicinity of the central suclus. Our method makes a few a priori assumptions: The regions around the central sulcus are adequately sampled and the occipital or parieto-occipital regions are not included in the analysis. In order for the method to function properly, nonsensori-MC should be sampled adequately as well. In the future, normative data could be generated for the composite product of connectivity × power which may replace within-patient z-scoring. Our method is rapid and can be implemented on short segments of

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