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Digital revolution in depression: A technologies update for clinicians

Max A. Lazar[a], Zihang Pan[a,b], Renee-Marie Ragguett[a], Yena Lee[a,b], Mehala Subramaniapillai[a], Rodrigo B. Mansur[a], Nelson Rodrigues[a], Roger S. McIntyre[a,b,c,d,⁎]

[a] Mood Disorders Psychopharmacology Unit, University Health Network, University of Toronto, Toronto, ON, Canada
[b] Institute of Medical Science, University of Toronto, Toronto, ON, Canada
[c] Department of Psychiatry, University of Toronto, Toronto, ON, Canada
[d] Department of Pharmacology, University of Toronto, Toronto, ON, Canada

ABSTRACT

Technology is becoming increasingly intertwined with our lives every year. As technology advances, it offers promising new methods to help detect, manage, and improve the care of major depressive disorder (MDD). Unlike other specialties in medicine, psychiatry has been slow to adopt new technologies. Other areas of medicine, primarily cardiology and oncology, have made use of technological methods to patients' great benefits. In psychiatry, new technological methods can predict which antidepressants will be most effective, provide therapies to patients, and empower patients to manage their own medical records. We offer an overview to new technologies and their applications to psychiatry for novices. Our particular focus is big data, machine learning, mobile applications, and blockchain technology. We summarise the uses of technology as assisting physicians in decision making, facilitating patient-patient interaction, and securely storing and managing health-care data. We suggest possible advantages and challenges to adopting these methods. Continued research and technological innovation is needed to improve the psychiatrist's toolbox and to monitor the adoption and consequences of new technologies.

Introduction

Technology is becoming increasingly present in our lives with each passing year. In 1977, Ken Olson (founder of the Digital Equipment Corporation, which later became Hewlett-Packard) said that there is no reason anyone would want a computer in their home [1]. As an alternative to Olsen's prediction, Gordon Moore, cofounder of Intel, expected technology would become increasingly more complex and increasingly available. Moore's Law, named after Gordon Moore, predicts that technological complexity will rise exponentially, which corresponds with a rise in information processing capacity [2]. Indeed, as predicted by Moore, our ability to store and communicate information has risen in the forty years since 1977. In 2017, there is ubiquity in ownership of personal computing devices with immense storage and communication capabilities.

The digital and data revolutions are relatively recent phenomena. In psychiatry, computational methods are being increasingly adopted by research and clinical ecosystems in novel ways. With the addition of many pieces of data for each patient (e.g. genomic, metabolomic, magnetic resonance imaging, etc.), psychiatry has needed to turn to more sophisticated bioinformatic solutions given these large data sets. The methods of big data and machine learning (ML) are enabling psychiatrists to effectively integrate large amounts of patient data and recognize interactions between variables (e.g. environmental and genetic risk factors). Medical apps and online paramedical communities (e.g. Facebook groups, blogging communities, etc.) are facilitating patient-patient interaction and changing the ways in which patients approach the treatment of psychiatric disorders. New cryptographic methods could be used to integrate and secure patient health care data, resulting in better secured data that is easily shared between healthcare providers and their patients. In this paper, we synthesize recent technological developments as they apply to clinical psychiatry and outline some of the ways that these methods may be used by clinicians now or in the very near future. Finally, we note some of the difficulties in incorporating these new technological methods into clinical practice. Many of the complications stem from the need to trust in the capabilities of these methods before they can be brought standard treatment for mood disorders.

⁎ Corresponding author at: Mood Disorders Psychopharmacology Unit, University Health Network, Toronto Western Hospital, 399 Bathurst Street, 9th Floor – Main Pavilion, Toronto, ON M5T 2S8, Canada.
E-mail address: roger.mcintyre@uhn.ca (R.S. McIntyre).

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Big data and machine learning

Big Data is a term that refers both to large datasets and the statistical analysis of this type of data Traditionally, big data has been described by the three V's: volume, velocity, and variety [3,4]. These three factors refer to the size of datasets, the rapidity with which data is acquired, and the differing sources and types of data that are used in these projects. The Large Hadron Collider (LHC) at the Centre for European Nuclear Research (CERN) may serve as an example. The LHC generates about 1 PB (1 million gigabytes) per second [5], which data on includes particle trajectories, calorimetrics, and classifications. The data generated by the LHC certainly meets the dataset criteria for big data. Big data is also created through mobile phone monitoring by our daily routines, such as: our call activity, internet browsing history, location, exercise data (e.g. steps walked, heart rate, sleep time, etc.). This data is collected and associated with each of us, and in some cases shared amongst us, contributing to not only big data, but also deep data. Such data is now used as an integral component of the consumer analytics that offer us individualized advertisements on the internet.

Big data necessitates new statistical methods for data analysis. Among these methods, machine learning (ML) is one of the most popular [6]. Machine learning employs algorithms to establish relationships between variables in the multidimensional dataset, called a training set. These established relationships are often validated against a second set of data. After the validation process, ML algorithms can be used to predict future results given the information that was determined from the training dataset. A subset of ML techniques fall into the category of deep learning, which are characterized by inputting data without classification and using nonlinear functions to remove unwanted information. Methods in machine and deep learning are of particular interest in medicine as they allow the comparison of new patients to larger populations to aid in treatment, risk assessment, and other clinical decisions.

While big data and ML are present in many areas of medicine, both in research and clinical settings, clinical psychiatry has been relatively slow to adopt and implement these methods. Nonetheless, there are some recent applications that hold promise. Recent work with big data and ML techniques have provided the basis for risk stratification in psychiatry. Risk stratification is the determination of a patient's risk for a particular condition and need for preventative interventions. Risk stratification has already been used for decades in specialties like cardiology, oncology, and nephrology [7–9], and now its application to psychiatry is providing novel insights to assess the persistence and severity of depression [10], risk of suicide [11], likelihood of treatment-resistant depression [4,12], and response to drug therapies [4,6,13–16]. In addition, machine learning has also been used in efforts to elucidate potential biomarkers for mental disorders [17,18]. Of particular interest for clinicians are web-based tools, the likes of which have been described and designed by Perlis [12], which allows clinicians to input basic information drawn from the 16 question Quick Inventory of Depressive Symptomatology (QIDS-SR16) to predict the likelihood of treatment-resistant depression when compared to the Sequenced Treatment Alternatives to Relieve Depression study (STAR*D) cohort. The tool is available for free online use at http://trdrisk.mghcedd.org/. Perlis showed that the QIDS-SR16 provides a meaningful result and that the risk stratification tool has a prediction area under curve (AUC) of 0.714 [12]. The AUC is a single metric that combines both the sensitivity and false positive rate of a classification tool. In order to be calculated, both the sensitivity and false positive rates are computed with many different thresholds (e.g. 0.00, 0.01, 0.02, …, 1.00). The results of these calculations are then graphed (with sensitivity on the ordinate axis) for a logistical regression. The curve created is referred to as the receiver operating characteristic (ROC) curve. The area under the ROC curve is the AUC that is associated with the classification tool. Prediction area under the curve values close to 1 and far from 0.5 indicate strong predictive power. The AUC that Perlis obtained for his risk stratification tool (0.714) is above some prediction tools commonly used to stratify risks in cardiology [7], oncology [8], and nephrology [9]. For instance, one of the most widely used and widely-studied risk stratification algorithm for breast cancer, the Gail score, has an AUC between 0.56 and 0.67 [8].

In addition to risk stratification tools, one of the most promising clinical applications of big data and ML is treatment selection for patients with MDD. There have been multiple studies in this regard. One algorithm, Created by Gordon et al. [19], was able to make strong enough individual treatment predictions that resulted in number needed to treat (NNTs) of 2–5. Median NNTs for tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRI) are 9 and 7 [20]. The NNT describes the average number of patients needed to be treated to prevent an additional poor outcome (in this case, lack of remission). The NNT can equivalently be described as the number of patients that needed to be treated for 1 patient to benefit, as compared with a control in a clinical trial. An ideal NNT would be 1, where every patient benefits from the treatment. Given the novelty of these techniques, only one study thus far [15] has tested their proprietary algorithm through a 12 week-long randomized trial in a clinical setting, with promising results. Using an EEG database of 1800 individuals comprising 17000 treatment attempts, the proprietary ML algorithm of DeBattista et al. outperformed clinical judgement insofar as reduction of QIDS-SR16 and Quality of Life Enjoyment and Satisfaction Questionnaire-Short Form (Q-LES-SF) scores at the end of the trial. The study found that by week 12, the reduction in QIDS-SR16 scores in 65.0% and remission (QIDS-SR16 score less than 5) in 35.0% of protocol population (compared with 38.8% and 26.5% in the control group) at $p < 0.0002$ [15]. These statistics translate to a NNT 4.1 using the study algorithm. Furthermore, in the protocol population, there was a significant reduction in agitation and anxiety, which are statistically significant predictors of suicide ideation and attempts [21]. However, the algorithm of Debattista et al. frequently recommended the use of monoamine oxidase inhibitors (MAOIs). The algorithm seems not to account for the risk of fatal drug and diet interactions involved with MAOI use [22,23]. Furthermore, the algorithm occasionally indicated the use of rarely used treatments. In one case, the algorithm recommended the use of propranolol, which has little evidence of being an effective pharmacotherapy for mood disorders [24]. Further modifications to algorithms, such as allowing a physician to indicate that MAOI use is not appropriate for the patient, may be needed before ML algorithms can confidently be adopted into standard prescribing practice.

Additional limitations of the foregoing studies partly reside in the lack of large participant datasets in psychiatry. There are very few large-scale studies of depressed patients. The STAR*D cohort is perhaps the best known, but is already 10 years old. As a result, many of the ML approaches to big data have had to artificially divide data from the same cohort into training, validation, and testing sets. The concern with using the same study for both training and testing is overfitting. Overfitting (shown in Fig. 2) occurs when algorithm is perfectly able to match the data it is given, including any noise, confounds, and bias that may be present. When the training and testing sets are both part of the same larger superset, noise, confounds, and bias are not removed between the two sets. Accordingly, the algorithm may have poor ability to generalize to a clinical populations which may differ from study populations.

Due to problems in algorithms and their generalizability, it is important to moderate technological optimism. At this stage, the relationship between big data and psychiatry is nascent. As such, these techniques are promising (and in some cases ready for use), but must be used concomitantly with clinician judgement. The use of ML is not meant to replace clinicians, but to augment and compliment their assessments and decision making. For example, the algorithm of DeBattista et al. [15] may recommend the use of MAOIs for a particular patient. The clinician is then needed to assess the risks associated with

MAOI use in that patient. Thus the future of ML in psychiatry will depend on the ability of algorithms to make suggestions and clinicians' ability to weigh those suggestions against their judgement.

Medical apps and online paramedical communities

Clinicians have witnessed the proliferation of more sophisticated data analytic tools. Apps for mood disorders seem to fall into four main categories: (1) Assessments of self-report measures of depressive symptom severity (PHQ-9, HDR, etc.), (2) Recording and tracking mood and biological data (e.g. sleep time, heart rate, etc.), (3) Augmenting clinical care (i.e. remind patients to take and refill their prescriptions), and (4) Providing internet-delivered CBT (iCBT). Of these tools, the most popular seems to be MoodGYM, a free app offering iCBT [25,26]. While these apps alone may not be enough to achieve remission, they offer meaningful support at the population level and provide the first steps towards seeking professional help. Unfortunately, possibly due to the lack of personal interaction [27], adherence to internet-based tools is fairly low (e.g. as little as a 10% retention rate for users of MoodGYM [28]). Despite problems with adherence to iCBT, this intervention functions well as a population-level intervention. Though iCBT may only benefit a small proportion of users who adhere to the program, a small proportion of the user base may amount to a substantial number of people.

In addition to apps, motivated persons may seek other internet-based supports. Tumblr is a relatively popular social media platform that affords their users some degree of anonymity and has large communities mobilized around mental health. The anonymity and lack of supervision in these paramedical communities offer the opportunity for users to discuss their conditions openly and share jokes relating to the experiences of living with mental illness. An internet search (see Appendix B. Social Media Search and Inclusion Strategy) revealed that Facebook also has groups and pages dedicated to provide support and share stories for members with mood disorders. Furthermore, a general Google search displays in hundreds of thousands of online non-institutionally authored mood disorder forums that fill the same role. Complimentary media platforms such as YouTube also have videos aimed at individuals struggling with depression. There is evidence to suggest that these online clustering interactions have beneficial effects [29–31]. However, there is a marked risk in both self-diagnosis [32] with a mood disorder and the normalization of depression risk behaviours such as suicidal ideation and self-harm [33].

In a recent analysis of Tumblr content, Cavazos-Rehg et al. found that, of depression-themed blogs studied, a significant portion (18%) contained graphic images or video-clips of self-harm behaviours [33]. In addition, while 41% of interactive posts (Tumblr asks) provided positive or supportive advice, 25% of interactive posts provided potentially harmful advice, such as how to hide serious maladaptive behaviours (e.g. self-harm) from others [33]. In addition, only 13% of interactive posts suggested professional help in combating depression [33].

While the aforementioned statistics are limited in that they represent a subset of a posts over a specific subset of time, we ought to be aware of the ways in which people interact online that may contribute to the worsening of their depression. The effect of social media content on risk factors for mood disorders is a novel area of research. Given the large number of paramedical communities dedicated to depression, further research is needed to ascertain the effects of "depressive paramedical communities" on depression symptomatology and risk. If there is a positive significant association between the "depressive paramedical communities" and depression risk, we must examine and discuss the role of physicians in combatting the normalization of depression risk behaviour by social media platforms. By the same token, we will have to examine the ways in which social media facilitates positive effects in the lives of those with mood disorders. This too merits further study as social media platforms grow and gain new user bases. Overall, the risks and benefits of social media in mood disorder patients will need to be weighed and new treatment recommendations could emerge. However, as these studies are merely preliminary, we will need more data to ascertain the role of paramedical social media groups in depression.

As a result of the internet-based tools available to patients, the treatment landscape is changing. Patients often interact with each other in relatively anonymous spaces – both for better and for worse. That said, clinicians (and in particular family physicians) may be able to use some of the app-based tools to their advantage while their patients wait to see a psychiatrist or other clinician.

Blockchain

Blockchain is a decentralized data management technology that was first developed for the use of bitcoin cryptocurrency in 2008 [34]. Blockchain works by maintaining a public ledger system of transactions that is available to all computers in the sharing network. Each computer in the network is known as a nodes. Every piece of information is stored in time-stamped blocks that contains a link to the block before it. The information is subsequently stored in a chain of timestamped blocks, each linked to the one immediately succeeding and the one immediately preceding it. This ledger system stores every transaction ever made and is verified continuously by each node in the network. While many applications of blockchain have focused on bitcoin and other cryptocurrencies, there is a growing potential for medical applications, particularly in the field of managing and storing patient health records [34,35]. The use of blockchain technology in medicine is still in its infancy, and as such, there are few studies to identify applications and evaluate the efficacy of blockchain technologies in medicine. Excitement in this field may promise more clinical applications within the coming years.

One particularly exciting application is the combination of cloud computing and blockchain technology in the secure management and storage of electronic health data. In one such system proposed by Yue et al., pieces of data are securely stored in a blockchain cloud, managed and owned by patients, and voluntarily shared with data users [35]. In their app, Yue et al. take advantage of blockchain's ability to provide auditable computing applied to the secure and accessible storage of healthcare data. The organization eliminates the issue of fragmented patient health records, and the violation of a patient's privacy as the patient is the owner of their own healthcare data. This data may then be encrypted and sent to third parties, such as physicians, researchers, government agencies, or others requesting data access. For example, if a patient's psychiatrist refers them for bloodwork, the patient receives the bloodwork results. It is the patient who is the ultimate owner of their own healthcare data. The patient may then securely send a copy of their results to their psychiatrist for review. Patient ownership of their own healthcare data may help to disassemble information silos and remedy a lack of communication between healthcare teams. As it stands, the family physician is often intended to be the primary manager of a patient's data, however they may be left out of the loop during their patient's referrals and hospitalization. Under such a system as Yue et al. propose [35], everyone shares the same information.

The secure, patient-centred organization of healthcare data is particularly relevant when considering the proliferation of ML technology to psychiatry. Many ML algorithms require large data inputs, including blood work, patient history, MRI results, etc. In order to successfully use ML algorithms to assist in the treatment of patients, we need access to these large datasets. The more accessible the data is to clinicians, the easier it is to use.

The applications of blockchains are exciting and suggest that they will be able to securely manage healthcare data. However, in the present, proliferation of blockchain based-medical information storage has been slow due to concerns over a number of key technological issues. These key issues, described by Swan [36] include:

Speed: Blockchain networks perform transactions very slowly, which results in very slow data exchange and writing. For comparison, the Bitcoin network is maximized to perform 7 tps (transactions per second), whereas the Visa and Twitter networks perform 2000 tps and 5000 tps [36].
Size: Blockchain networks grow very quickly and subsequently require large amounts of bandwidth. It is expected that if throughput issues are resolved, blockchain in the bitcoin network could grow by 214 PB (214 million gigabytes) annually [36].
Security: Current blockchain may be vulnerable to a 51% attack. In this type of attack, a single entity gains control of the network. Some chains are more vulnerable to 51% attacks than others. A 51% attack is a particularly pertinent issue when either money or sensitive information is involved.

Blockchain may have the potential to revolutionize the way patient data is stored, but more of its technical issues must be resolved before it can safely be adopted to consolidate medical data. Furthermore, the relationship between blockchain and medicine has yet to fully emerge. However, It remains to be seen what blockchain may promise to clinical practice.

Conclusions

In order for these aforementioned newer technologies to be effective, they must cater to the use by clinicians. As they stand, ML technologies remain opaque to many, and often require advanced technical knowledge in order to design, interpret, and troubleshoot. As such, these tools must be designed for use by clinicians who are instructed on how to interpret the data outputs. In addition, we need more clinicians who are willing to collect data on patients. Private practice psychiatrists may be hesitant to devote patient time to measurements such as taking MADRS scores and running calculations. However, to be used to their fullest effect, ML techniques are best used by all clinicians to assist in the treatment of their patients.

Along the same line of thought, psychiatry needs more data. We have very few long-term cohort studies, save from the International Study to Predict Optimized Treatment – Depression (iSPOT-D) and STAR*D, and they are aging fast. In addition, these studies are prone to the sort of systematic error that occurs when measurements only exist for those participants who completed the studies. These are the rarefied sorts of patients who may not accurately comprise the general population seeking psychiatric treatment. As a result, to increase the precision of the ML algorithms, we need better representative data and we need more of it.

For a final consideration, we need more effective ways to use technology in the treatment of patients with multiple comorbid conditions. Current ML diagnostic classifications do a poor job of distinguishing between two comorbid diseases and may be unable to accurately help diagnose or safely prescribe to patients with comorbid diseases.

In light of these issues, the potential payoff is huge. Using ML, we may be able to treat patients much more effectively. Diagnosis may become easier, but more importantly, treatment may become more effective and patients may suffer less. We may see the end of days when the average patient fails three consecutive pharmacotherapies.

Author contributions

RSM suggested the topic for the manuscript. The literature search was conducted by both MAL and RSM, and the preliminary draft was written by MAL under the supervision of RSM. Data collection and figures were made by MAL. All authors contributed equally to the subsequent editing and revision of the manuscript.

Conflict of interest statement

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Ethics

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Appendix

See Fig. 1.

Methods

Search strategy and selection strategy

Electronic searches were performed on PubMed using combinations of the MeSH terms (“depressive disorder” and one of the following: “machine learning” OR “mobile application”). Since MeSH terms do not exist for “big data”, “deep learning”, or “blockchain,” they were also included as keywords in the search criteria. Articles published in languages other than English were excluded. No time restrictions were placed on articles. Articles were reviewed by ML and selected for inclusion if they were deemed to be relevant to the area of emerging technologies in psychiatry. Any uncertainties were reviewed by ML and RM.

Social media search and inclusion strategy

We drew from previous social media studies in medicine [37,38]. Manual electronic searches were performed by ML in Google, Tumblr, Facebook, and YouTube. All searches were conducted during March 2017. The search strategy used combinations of the keywords (depression OR MDD OR support OR group OR forum OR coping OR remission OR recovery). Admission criteria for searches was given by

1) Published online
2) Contains information relating to depression

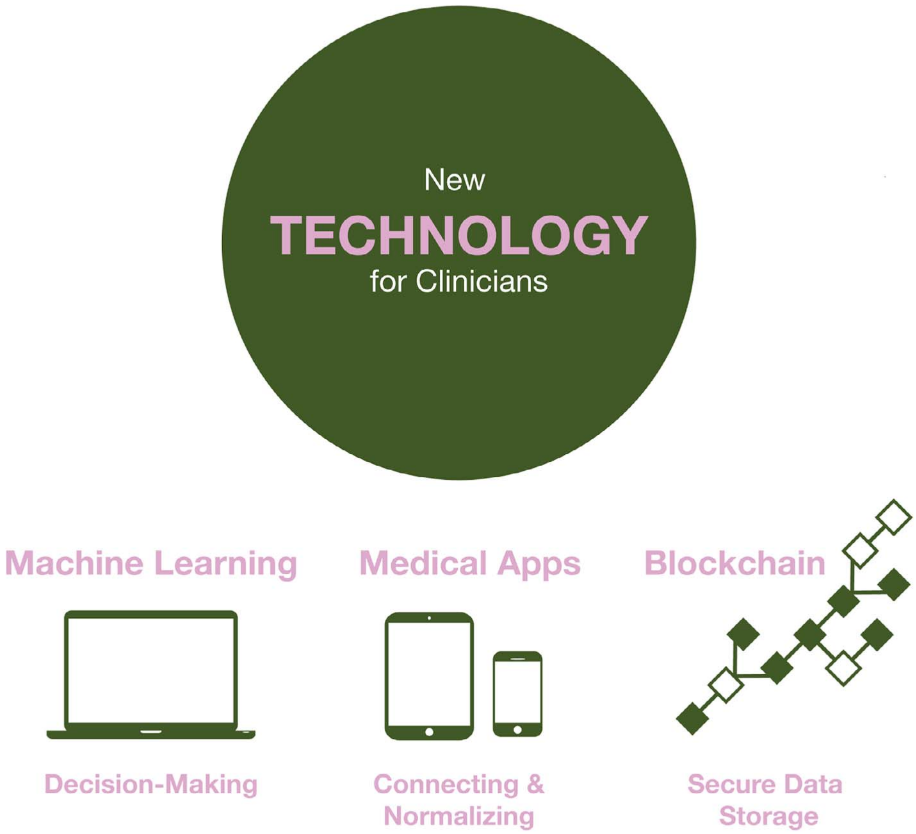

Fig. 1. An overview of the technologies surveyed in this paper.

3) If published as an online forum, contains ≥1 response to the original post
4) If published as a Tumblr blog, contains ≥100 followers
5) If published as a Facebook group, contains ≥10 members
6) If published as a YouTube video, has been viewed ≥100 times

Websites/platforms were excluded if

1) They were not published in English
2) Were authored by an institution or research group

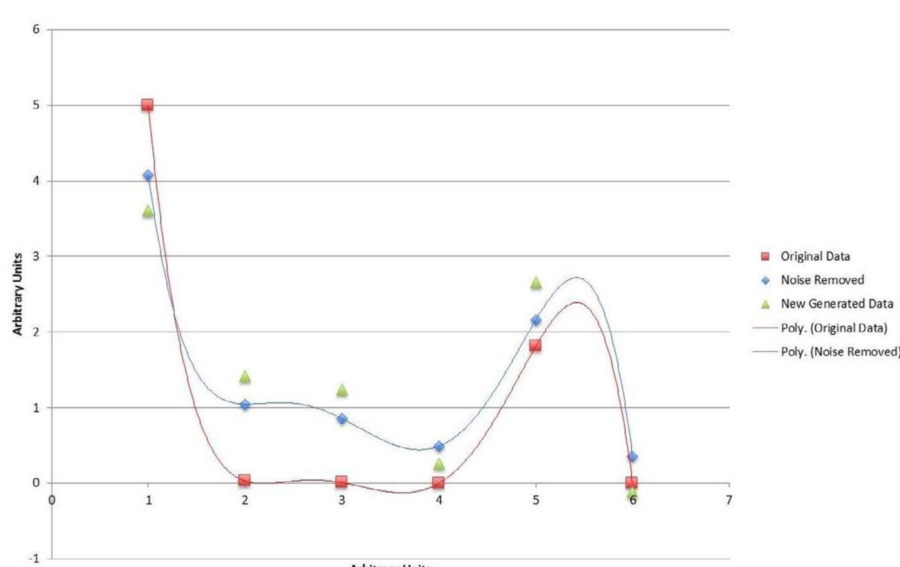

Fig. 2. An example of overfitting. Randomly sampled data (square) is used to create a polynomial fit (line between square data points). Note that the 6 data points perfectly describe a 5th order polynomial. Once transformed to remove noise, the diamond-shaped data points and their polynomial fit (line linking the diamond-shaped data points) differ significantly from the observed data. Once new data points (triangles) are measured, they are not well explained by the untransformed square model. The square model demonstrates overfitting.

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