Among addictive disorders, alcohol dependence is arguably the most common and disabling disorder and is often difficult to treat. Popular belief suggests that alcohol dependence is a matter of will power or lack of spirituality. Although cognition and social support play an important role in the treatment of addiction, neuroscience continues to shed light on other aspects of this disease. What is clear is that alcohol dependence is a heterogeneous disorder with many contributing factors. These factors vary from person to person and are known to have a major impact on treatment outcome. This variability, in part, has contributed to the development of new treatments. These treatments vary in their approach and range from psychosocial interventions, such as housing and employment focused care, to cognitively based approaches using cognitive behavioral therapy, to peer and spirituality based approaches and to pharmacological approaches. Research gains in understanding the heterogeneity of addiction coupled with the availability of a wide range of treatments have opened the door to the possibility of personalized approaches to treatment. The goal of a personalized or tailored approach to treatment planning is to maximize outcomes in the treatment of each individual and not just offer one standard treatment or treatments.

The basis for personalized medicine rests in the realization that addiction is a complex disorder. The principle neurological components of addiction include the acute and chronic response to alcohol, a variety of craving states, affective response and drive and executive control. The challenge of personalized medicine is to identify the various components of addiction that are relevant to an individual in a way that treatment can be tailored. One avenue of bringing the scientific advances to the bedside has been to develop biological markers that map to these critical components of addiction. While traditional biomarkers have been used for monitoring treatment outcomes, biomarkers that associate with neurological function have the potential to facilitate tailoring or personalizing treatment as these biomarkers may represent intra-individual differences in the underlying vulnerabilities to addiction. So far, neurological biomarkers have focused on genetic biomarkers, neuroimaging markers and physiological markers. Laaksonen et al. (2011) (this issue page 308) describe the association between sweet testing and response to naltrexone. Sweet liking is genetically determined and has been shown by others to have some relationship to alcohol consumption. In theory, sweet testing may provide a window to understanding olfactory and gustatory cues and preferences for substances like alcohol. Other recent and promising biomarkers include work done with neuroimaging. Several different studies have shown value in using positron emission tomography (PET) or functional magnetic resonance imaging to understand cue-induced craving and executive control of responses to cues (Childress et al., 2008; Franklin et al., 2007; Myrick et al., 2004).

Genetic testing has taken the biomarker field by storm. Not only do genetics and proteomics offer an in-depth look at the biology of the brain, but also these tests have the advantage of being easily disseminated and adapted into clinical practice at a relatively low cost. If for example, it was possible to use genetic testing to predict a greater likelihood of positive response to a medication, it would be possible to use the medication with greater certainty and efficiency. This is the basis of recent efforts in the field of pharmacogenetics and alcoholism (Evans and Relling, 1999). Such a pharmacogenetic approach to treatment has economic implications by increasing the cost effectiveness of personalized medicine. Perhaps, more importantly, such an approach could also reduce the likelihood of unnecessarily exposing patients to a treatment that will be ineffective for them.

One area of particular promise is the work being conducted by multiple investigators studying the genetic variability in the μ-opioid receptor. It is widely known that μ-opioid neurotransmission is involved in craving and reward from a variety of substances including alcohol. Work in the past few years with existing databases from naltrexone studies has suggested that alcohol-dependent patients with one or two copies of the Asp40 variant in the μ-opioid gene had significantly better treatment response, as measured by the absence of any heavy drinking (73.9% response), than patients with the Asn40 variant (49.0% response) (Oslin et al., 2003). The response rate among subjects homozygous for the Asn40 allele showed relapse rates on naltrexone (51.0%) that were only marginally better than those reported for placebo in combination with psychotherapy. This finding was replicated in analysis of participants in the NIAAA sponsored COMBINE study (Anton, 2008). In the COMBINE study, 87% of subjects who had one or two copies of the Asp40 allele had a positive outcome to naltrexone treatment compared with 49% response among those who were homozygous for the Asn40 allele. While these two studies have shown promise, other studies have not demonstrated this effect. Most notably, the association with Asp40 allele was not found in retrospective analysis of the VA Cooperative study of naltrexone (Gelernter et al., 2007). These studies have generated a new way of thinking about treatment of alcoholism but have also generated many questions. Our research group and other groups are now conducting research prospectively randomizing individuals by genotype. We are also examining the effects of alcohol ingestion among those without an Asp40 allele. Most notable is separate work by Ray and Oslin, (2009) and Plebani and Oslin, (in press) questioning the efficacy of naltrexone in those of African descent, which is a population known to have a very low allele frequency for the Asp40 allele.
The question remains as to when biomarkers will be used in clinical practice to steer treatment choice. To achieve this goal, not only will patients and providers need to embrace this change, we will need to better understand how to implement and disseminate biomarkers into clinical practice. Practical issues such as availability and cost will be sorted out while the more difficult task may be to change the culture of addiction treatment. For example, despite evidence for the efficacy of medications, such as naltrexone or acamprosate, these medications are seldom used in treatment. Indeed, antidepressants and ‘mood-stabilizers’ are the mainstay of pharmacological treatment despite very little evidence supporting this practice. The same observation can be made regarding evidence-based psychotherapies which are also seldom used in practice with rigorous attention to fidelity. Despite the challenges of implementation, biomarkers such as genetic testing and sweet testing offer substantial hope that personalized medicine may one day be a reality for treating persons suffering from addiction.

REFERENCES


Plebanji JG, Oslin DW et al. (in press) Examining naltrexone and alcohol effects in a minority population: results from an initial human laboratory study. *Am J Addict*