2011

Application of the Hill Criteria to the Causal Association between Post-Traumatic Headache and Assault

Michael D. Freeman
Oregon Health & Science University

Sean S. Kohles
Portland State University

Citation Details

Freeman, Michael D., and Sean S. Kohles. "Application of the Hill criteria to the causal association between post-traumatic headache and assault." Egyptian Journal of Forensic Sciences 1.1 (2011): 35-40.

Egyptian Journal of Forensic Sciences (2011) 1, 35–40

Forensic Medicine Authority

Egyptian Journal of Forensic Sciences

www.sciencedirect.com

ORIGINAL ARTICLE

Application of the Hill criteria to the causal association between post-traumatic headache and assault

Michael D. Freeman [a,b,*], Sean S. Kohles [c,d]

[a] Department of Public Health & Preventive Medicine, Oregon Health & Science University, Portland, OR 97239, USA
[b] Institute of Forensic Medicine, Faculty of Health Sciences, Aarhus University, Denmark
[c] Reparative Bioengineering Laboratory, Department of Mechanical & Materials Engineering, Portland State University, Portland, OR 97201, USA
[d] Department of Surgery, Oregon Health & Science University, Portland, OR 97239, USA

KEYWORDS

Forensic epidemiology;
Forensic biomechanics;
Biostatistics;
Causation

Abstract Post-traumatic headache (PTH) is a common and disabling symptom secondary to the traumatic event. It is known that assault is associated with a wide range of physical symptoms including PTH. In this work, the general causation approach provided by the Hill criteria is described as an assessment tool for specific causation with regards to PTH and sexual assault. Time-dependent models of probability and, in-turn, relative risk are described as quantitative algorithms for addressing inductive and abductive conclusions of causation in forensic science.

1. Introduction

Post-traumatic headache (PTH) is a difficult condition to evaluate epidemiologically because of variations in presentation, evaluation, definition, and pathogenesis. It is readily accepted that patients with direct head trauma may develop persisting headache, with approximately 15% of such patients with mild head injury complaining of PTH at 3 months.[1] PTH has been identified as frequent chronic pain sequelae of assault, including that of sexual assault.[2] In a study of chronic pain in a community sample of 292 women who had recently separated from their abusive partners (< 20 months), more than one-third experienced high disability pain including PTH as measured by Von Korff's Chronic Pain Grade.[3]

Headache is also a prominent feature of neck injury resulting from physical trauma including whiplash trauma resulting from car crashes.[4,5] In a recent report of the random sampling of 30–44 year-old Norwegians, the annual rate of chronic headache due to whiplash trauma or post-traumatic headache was found to be nearly the same, with around 1 in 260 suffering from one or the other.[6] Post-concussive symptoms may persist after mild head injury as indicated in a report from a clinic in the United Kingdom where the common complaints were ranked as fatigue,

* Corresponding author. Address: 1234 SW 18th Ave., Suite 102, Portland, OR 97205, USA. Tel.: +1 971 255 1008, mobile: +1 503 871 0715.
E-mail addresses: forensictrauma@gmail.com (M.D. Freeman), kohles@cecs.pdx.edu (S.S. Kohles).

2090-536X

Peer review under responsibility of Forensic Medicine Authority.
doi:10.1016/j.ejfs.2011.04.008

Production and hosting by Elsevier

headache, dizziness, irritability, sleep disturbances, poor concentration and poor memory.[7]

Because PTH is at times allegedly due to the negligence or malfeasance of another individual, and the condition is rarely captured by medical imaging and other conventional means of identifying injury (unless there is fracture or intracranial bleeding), there may be polarization of expert opinions regarding the most probable cause of the headaches. A treating clinician will most typically take a history from the patient, and if they have new headache complaints that they did not have prior to the injury event then an attribution of causation is made. An expert who is defending against a claim of chronic injury may find in the pre-trauma history of the patient prior complaints of headaches, and thus conclude that the onset of the headaches only coincided with the trauma, and that the trauma did not alter the natural history of the headaches. Fact finders are thus left at an evidentiary impasse, without a standard by which to compare the validity of the conflicting opinions.

A large part of this difficulty is the lack of general familiarity amongst those trained in forensic and clinical medicine with the standards of epidemiologic (general) causation, and how they may be systematically applied in cases of specific (individual) causation. The objectives here are to describe these criteria and how they may be used in a forensic setting to evaluate disputed causation in a case of alleged post-traumatic headache resulting from physical assault or another cause in which fault is due to the negligence of someone other than the victim. In addition, a time-dependent probability models are presented as a means to quantify relative risk. Such means of quantifying causal probabilities are important tools in forensic science.

2. Causal association

A broadly accepted definition of causation is that a specific event serves as an antecedent event or condition that was necessary for the occurrence of a specific disease or injury at the moment that it occurred, given that other conditions are fixed.[8] In other words, the cause of a disease or injury event is an event or condition that preceded the disease or injury and *without which the disease or injury would not have occurred (at the time at which it occurred)*. The scientific basis for general and specific determinations of cause and effect were introduced through the rules set forth by the philosopher David Hume and the inductive writings of John Stuart Mill in the 18th and 19th centuries, respectively.[9,10]

In the current era, a practical approach to causation was described in a systematic fashion by Sir Austin Bradford-Hill in 1965.[11] Hill outlined nine criteria by which population-based determinations of cause and effect could be made when there is substantial epidemiologic evidence linking a disease or injury with an exposure.[12] The Hill Criteria have served as the seminal basis from which virtually all subsequent systematic approaches to general (population) and specific (individual) causation have been derived, including those for a variety of injuries such as traumatic brain injury, carpal tunnel syndrome, needle stick injuries, and spinal disk injuries, among others.[13–16]

Hill's original nine criteria are as follows:

1. *Strength of association*: A strong association is more likely to indicate a causal relationship than is a modest or weak association. Strength of association is generally considered to be the most important determinant of causation. Most simply stated, a strong association is more likely to indicate a causal relationship than is a modest or weak association. Strength of association can be measured in general causation by the percentage decrease of an illness or injury in society if the injury cause were to be eliminated.[8] This is also known as the *etiologic fraction* that the particular cause contributes to the total societal burden of the disease. Strength of association is typically assessed by *relative risk* (RR), in which the risk of the injury or disease associated with the suspected cause is evaluated and compared with all other possible causes, and given as a ratio. An RR of >2.0 is the equivalent of a probability of causation of $>50\%$, meaning that it is more probable than not that the suspected causal relationship is true. An example calculation applying this metric to PTH and physical assault will be described in the next section.
2. *Consistency*: In general causation, the repetitive observation of a causal relationship in different circumstances strengthens the causal inference. For example, smoking different brands of cigarettes results in the same disease. Consistency may be said to be present in specific causation if other individuals have been observed clinically with the same outcome following substantially similar exposures.
3. *Specificity*: In general causation, specificity refers to the degree to which a factor is associated with a particular outcome or population. In his original paper, Hill discussed the rare condition of scrotal cancer among the unique profession of chimney sweeps as an example of specificity. Specificity is less a necessary factor for causation and more of a quantified variable of interest. For example, in a drug-related death, the drug may have a low specificity for death, as a very small proportion of deaths are caused by overdose of the drug, and the cause of death is often multifactorial. In contrast, a decedent found with a circular depression in his skull and a hammer nearby has an injury that is highly specific for a blow to the head with a specific hammer. Thus, specificity has value in specific causation when it is present, but a lack of specificity does not imply lack of causation.
4. *Temporality*: For this criterion to be satisfied, the potential causal factor must precede the outcome it is assumed to affect, and the outcome cannot either occur before it is physiologically feasible or after too great of a latency period. Temporality is the one factor that must always be present in general and specific causation in order to conclude that a cause and effect relationship is present.
5. *Biological gradient*: The injury outcome increases proportionately with increasing dose of exposure (also known as dose–response). This principle makes more sense when applied to general causation than specific causation, in that the fact that a lower dose of exposure will sicken or injure fewer people than a higher dose has little or no meaning to a causal investigation in the case of an individual who has fallen ill after a low dose.
6. *Plausibility*: For both general and specific causation, plausibility refers to the degree to which the observed association can be explained by known scientific principles. Hill did not put much weight in plausibility, having commented that a hypothesized disease cause that is thought to be implausible today may be found to be plausible at some time in the future as a result of new scientific inquiry. The

plausibility criterion is met when there is a *lack of established implausibility* (impossibility or 0% probability). For example, a brain tumor found via medical imaging on the day of a head trauma and loss of consciousness is implausibly related to the trauma due to the nature of the disease and injury mechanisms. A common error in specific causation is to consider a rare outcome to be the same as an implausible outcome. If a causal correlation is determined solely based upon the temporal association between an exposure and outcome, but implausibility is well established by a biologic disconnection, then the *post hoc ergo propter hoc* fallacy has been committed. Because the association is implausible, the inference of causation is fallacious. Just as important, however is the recognition of the false assertion of the *post hoc* fallacy, in which a rare outcome is improperly used as a basis to assert implausibility, and causation is improperly rejected in the presence of other criteria suggestive of causation.

7. *Coherence*: A causal conclusion should not fundamentally contradict present substantive knowledge – it should "make sense" given current knowledge. This is highly subjective; what does not make sense to one practitioner may make sense to another, depending on differences in clinical experience. Coherence is meant to be a liberal, rather than limiting criterion.
8. *Experiment*: In some cases there may be evidence from randomized experiments on animals or humans, although in most cases of injury there will not.
9. *Analogy*: An analogous exposure and outcome may be translatable to the circumstances of a previously unexplored causal investigation.

3. Application of the Hill criteria to post-traumatic headache and sexual assault

For practical determinations of specific causation of PTH in a forensic setting (cause and effect in individuals as evaluated for a legal matter) Hill's criteria can be grouped into two major forensic questions: criteria that answer the question "*could the exposure have caused the disease or injury outcome in this case?*" and those that answer the question "*did the exposure cause the disease or injury outcome in this case?*" To this end, Hill's criteria further grouped into three causal milestones, as follows:

3.1. Biologic plausibility

This criterion is meant to demonstrate whether or not the exposure *could* have caused the disease or injury outcome, regardless of how often, and is an amalgam of Hill's plausibility, coherence, consistency, specificity, biologic gradient, analogy, and experiment criteria. No single factor *must* be present to establish biologic plausibility, which simply means that the probability of a cause and effect cannot be said to be 0% (that it is implausible). As noted previously, an example of implausibility would be in which a brain tumor is discovered the day of a car crash and a head trauma. Clearly, it would be *implausible* to develop a brain tumor in a single day and as a result of trauma. In practice, this criterion is considered met if there is an absence of clearly established *implausibility*.

In applying the criteria that comprise biological plausibility to the evaluation of the relationship between persisting headaches and trauma, the first question that often arises is whether there is an injury force threshold for PTH. A number of authors have attempted to establish injury thresholds by pointing to the results of human volunteer crash testing and other activities that have been shown to be tolerable without injury. Such conclusions are based on logical fallacy, in that the demonstration that no injury is plausible in a selected population (that study subjects can tolerate a low speed crash without sustaining injury) is improperly generalized to the entire population by the sweeping conclusion that it is impossible to sustain injury in a low speed crash.[17] The epidemiologic concept of the asymptote, that there is no way to know at what point the *n*th most fragile member of the population falls on an injury probability versus traumatic force curve, dictates that implausibility cannot be concluded for virtually any degree of forceful loading of the head as a *possible* cause of PTH (Fig. 1). The conclusion begs the question (for some) as to whether a light tap on the head with a finger can cause PTH, and the answer is almost certainly not, but then again such a question would not arise in a forensic setting. For most clinicians, the recognition of the potential for injury of a described traumatic event in a patient's history is something like the well known quote of US Supreme Court Justice Potter Stewart regarding the definition of obscenity, that one "*knows it when one sees it*."[18] With no reliably established injury thresholds for PTH, the prevailing standard for judging plausibility is clinician common sense (the coherence criterion as described above).

Further, because of the lack of implausibility for PTH following virtually any traumatic head loading scenario or emotionally traumatic event (i.e. sexual assault), there is no need for the clinician to be able to quantify head loading forces in order to make an evaluation of plausibility in evaluating causation of PTH. As a result a *post hoc* biomechanical analysis of an injury mechanism may be helpful to fully describe *how* an injury occurred, such an analysis cannot be useful in a determination as to *whether* an injury occurred. Thus, an adequate history that there has been a head loading event during a sexual assault is adequate for the satisfaction of the biologic plausibility criterion.

3.2. Temporality

This criterion is the first step in establishing *whether* a biologically plausible exposure during an assault resulted in a case of PTH. Each case must be evaluated individually, but as a general rule, the headaches must start after the trauma and within a reasonable amount of time. In the case of a head trauma with a loss of consciousness, for example, a delay of one year from the last symptoms of head injury and the development of headaches would not be in keeping with a reasonable period of latency for PTH. On the other hand, headache is not always the first and foremost concern of a patient with a head injury following an assault, and thus a careful history is required to establish when the headaches began, relative to the time of the assault.[19] Some degree of headache is a highly prevalent finding in the general population; more than 60% of men and 80% of women will have experienced a headache in the year preceding an injury with the potential to cause PTH.[20] Thus it is reasonable that a patient who complains of headache

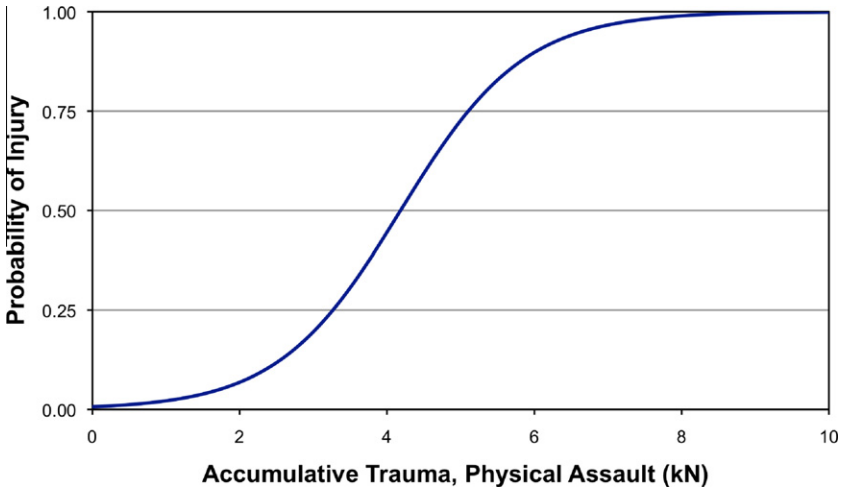

Figure 1 Hypothetical relationship between the probability of injury as associated with accumulated trauma during physical assault. The likelihood that anyone in a population of those experiencing large accumulated forces (and thus represented by a position on the curve as it asymptotically approaches 100%) would not be injured is considered *implausible*.

after a trauma has also experienced headache prior to the trauma. A careful history of the nature of the headache with regard to accumulated intensity, distribution, frequency, and duration both following and, if necessary, preceding a trauma is critical to determining if there has been a substantive change in a patient's history that is temporally associated with the trauma.

3.3. Strength of causal association

This is the final step in determining *whether* an exposure caused an injury outcome in which the risk of the condition relative to the suspected exposure is compared to the competing risk of the condition had the exposure not occurred, given the timeframe of the exposure. If a competing traumatic exposure has taken place then a comparison of dose may be appropriate, and the temporal relationship of the competing exposure must be compared to that of the exposure that is under investigation.

Often, the only other explanation for an injury or disease outcome aside from a suspected exposure is the coincidental onset of the condition (the probability the condition was going to occur at the same time regardless of the injury exposure). The comparison of the risk of the condition associated with the suspected exposure to the risk of the condition absent the exposure during the period of time that the exposure occurred is evaluated with the ratio between risks or probabilities, the relative risk (RR) as mentioned previously. For the clinician the quantification of RR is not typically feasible; but a qualitative assessment of competing risks can suffice in the place of the RR.

4. Relative risk as a quantitative metric for specific causation

The specific causation approach allows one to develop a mathematical definition of RR in order to answer the question "*did exposure A cause condition B ?*" by comparing all of the known and potential causes of B given the temporal relationship between A and B. Here, the probability that a condition B resulted from a "prime causal suspect" A_s out of n known alternative causes plus the influence of coincidence can be represented with the following RR calculation for the causal relationship of $(B|A_s)$:[21]

$$\text{Relative risk } (B|A_s) = \left(\frac{P(B|A_s)}{\sum_{i=1}^{n} P(B|A_{a^i}) + P\left(B|\frac{A_c}{t^2}\right)} \right) \tag{1}$$

in which $P(B|A_s)$ is the probability of the diagnosed condition B given exposure to prime causal suspect A_s; $\sum_{i=1}^{n} P(B|A_{a^i})$ is the sum of the risk of all known alternative plausible causes of B occurring in the same time frame as A_s as i goes from 1 to n alternative causes; and $P\left(B|\frac{A_c}{t^2}\right)$ is the probability of the coincidental occurrence of B per the time span between prime causal suspect A_s and the first clinical sign of condition B, designated as t. Taking into account the joint probability of the temporal alignment of the theoretically independent events A_s and B, the t^2 factor in the denominator represents the random match probability associated with coincidental cause A_c. The resulting algorithm provides a metric for assessing the relative nature of causal influences while taking into account the biomechanically or epidemiologically derived injury risk values in the numerator of the RR calculation as well as the duration of time between exposure to the prime causal suspect and the injury outcome.

The temporal relationship between a traumatic exposure and the development of PTH becomes the most important factor in evaluating the strength of the causal association between the two. This is primarily because the closer the temporal relationship between trauma and development of symptoms, the lower the probability that another unknown or unseen cause has coincidentally intervened. Time-dependent probabilities of association with specific trigger-events can be modeled by known biologically-relevant functions such that $P_T = P(B|A_s)$ for input into Eq. (1). These types of functions describe a hypothetical diminishing influence of the most probable association from an initial traumatic exposure (applied at $t = 0$) through time, and hence a temporal relationship.[22] A biologically relevant Gaussian (bell-shaped) distribution function can be used to describe a delayed or limited initial decrease in temporal association between a suspected injury cause and an injury outcome. The following mathematical relationship characterizes molecular diffusion coefficients

during nuclear magnetic resonance spectroscopy for medical physics applications including evaluation of traumatic head injury, but also can be applied to the time-dependant risk of PTH from assault:[23]

$$P_T = P_0 e^{-t^2/(2k_G^2)} \quad (2)$$

For the PTH scenario, the time constant k_G can be specified for the facts in a specific assault and P_0 is an acute baseline probability at $t = 0$, typically 100%, meaning that the maximum risk of acquisition of PTH is greatest right after the assault, and the risk decreases with time along a bell-shaped distribution (Fig. 2).

The relationships described in Eqs. (1) and (2) can be applied to make causal determinations of PTH relative to the timing of a traumatic exposure. In the patient who develops PTH within a matter of hours to days of a head trauma, unless the patient is a frequent and chronic headache sufferer prior to the traumatic assault, the temporal proximity is such that a coincidental onset of headache is far less probable than is a causal relationship between the injury and the PTH. In cases in which there is a greater period of latency between the trauma and the onset of headache, more scrutiny is required to assess the probability of coincidence, with particular attention paid to pre-assault history of headache. The question the forensic examiner must ask is "had the trauma not occurred, would one predict that these headaches would be present ?"

Unless this question can be answered yes then the RR favors the trauma as the cause of the headaches. A weighted odds ratio (OR), similar to the RR metric of Eq. (1), has been previously used to evaluate the general causal link between sexual assault and headache, while controlling for age and level of education. A mean OR = 1.70 (95% confidence interval = 1.40–2.07) indicated a statistically strong association between PTH and sexual assault.[2] A similar analysis has been performed on PTH secondary to trauma associated with warfare, with a finding of an OR = 2.25, indicating an association between combat-related physical assault and headaches (95% confidence interval = 1.17–4.33).[24]

In specific causation, strength of association is determined by the lack of *more* probable alternative or competing explanations, and this is somewhat different than in general causation. An example would be a death occurring 1 h following the administration of an intravenous drug. The death may be very rarely associated with the drug (e.g. 1 death per 100,000 doses), and thus the strength of association, relative to general causation, is very low (only a very small proportion of total deaths would be avoided if the drug became unavailable). However, if the probability that the other cause of death that would have been likely to act coincidentally between the time of the drug administration and the death (e.g. infection, sudden cardiac death, etc.) is even lower, then the relative strength of association of the drug to the death, in comparison to other causes, is very high. This concept of balancing or contextualizing the probabilities is the key to evaluation of specific causation.

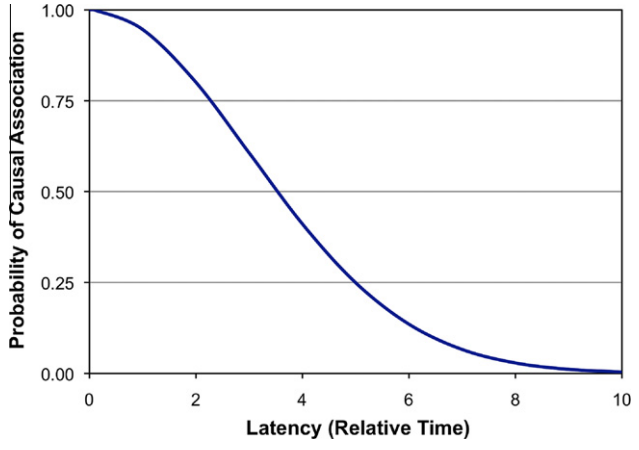

Figure 2 The modeled temporal association of specific causation between a physical assault (at time, $t = 0$) and PTH, during a given latency period. The Gaussian function of Eq. (2) was optimized such that $k_G = 3.0$ for the example scenario.

5. Conclusion

Determinations of cause and effect in forensic cases of headache following an assault and other trauma can be approached systematically as described herein. The most critical concepts for the forensic examiner to keep in mind is that of relative risk, and the important role that time between the trauma and onset of symptoms plays in dictating the strength of a causal relationship.

References

1. Blyth BJ, Bazarian JJ. Traumatic alterations in consciousness: traumatic brain injury. *Emerg Med Clin North Am* 2010;**28**(3):571–94.
2. Golding JM. Sexual assault history and headache: five general population studies. *J Nerv Ment Dis* 1999;**187**(10):624–9.
3. Wuest J, Merritt-Gray M, Ford-Gilboe M, Lent B, Varcoe C, Campbell JC. Chronic pain in women survivors of intimate partner violence. *J Pain* 2008;**9**(11):1049–57.
4. Faux S, Sheedy J. A prospective controlled study in the prevalence of posttraumat headache following mild traumatic brain injury. *Pain Med* 2008;**9**(8):1001–11.
5. Crutebo S, Nilsson C, Skillgate E, Holm LW. The course of symptoms for whiplash-associated disorders in Sweden: 6-month followup study. *J Rheumatol* 2010;**37**(7):1527–33.
6. Aaseth K, Grande RB, Kvaerner KJ, Gulbrandsen P, Lundqvist MB, Russell MB. Prevalence of secondary chronic headaches in a population-based sample of 30–44-year-old persons. The Akershus study of chronic headache. *Cephalalgia* 2008;**28**(7):705–13.
7. Haboubi NH, Long J, Koshy M, Ward AB. Short-term sequelae of minor head injury (6 years experience of minor head injury clinic). *Disabil Rehabil* 2001;**23**(14):635–8.
8. Rothman KJ, Greenland S. Causation and causal inference in epidemiology. *Am J Public Health* 2005;**95**(Suppl. 1):S144–50.
9. Hume D. *A treatise of human nature* [Originally published in 1739] [Oxford University Press edition, with an Analytical Index by L.A. Selby-Bigge, published 1888]. 2nd ed.; 1978 [with text revised and notes by P.H. Nidditch].
10. Mill JS. *A system of logic, ratiocinative and inductive*. 5th ed. London, England: Parker, Son and Bowin; 1862;
, Cited inClark DW, MacMahon B. *Preventive and community medicine*. 2nd ed. Boston: Little, Brown; 1981.
11. Hill AB. The environment and disease: association or causation? *Proc Roy Soc Med* 1965;**5**:295–300.
12. Morabia A. On the origin of Hill's causal criteria. *Epidemiology* 1991;**2**:367–9.

13. van Reekum R, Streiner DL, Conn DK. Applying Bradford Hill's criteria for causation to neuropsychiatry: challenges and opportunities. *J Neuropsychiatry Clin Neurosci* 2001;**13**(3):318–25.
14. Lozano-Calderón S, Anthony S, Ring D. The quality and strength of evidence for etiology: example of carpal tunnel syndrome. *J Hand Surg Am* 2008;**33**(4):525–38.
15. Batty L, Holland-Elliott K, Rosenfeld D. Investigation of eye splash and needlestick incidents from an HIV-positive donor on an intensive care unit using root cause analysis. *Occup Med (Lond)* 2003;**53**(2):147–50.
16. Freeman MD, Centeno CJ, Kohles SS. A systematic approach to clinical determinations of causation in symptomatic spinal disk injury following motor vehicle crash trauma. *PMR* 2009;**1**(10):951–6.
17. Freeman MD, Croft AC, Rossignol AM, Weaver DS, Reiser M. A review and methodologic critique of the literature refuting whiplash syndrome. *Spine* 1999;**24**(1):86–98.
18. Gewirtz P. On "I know it when I see it". *Yale LJ* 1996;105.
19. De Luca GC, Bartleson JD. When and how to investigate the patient with headache. *Semin Neurol* 2010;**30**(2):131–44.
20. Rasmussen BK, Jensen R, Schroll M, Olesen J. Epidemiology of headache in a general population – a prevalence study. *J Clin Epidemiol* 1991;**44**(11):1147–57.
21. Freeman MD, Kohles SS. An evaluation of applied biomechanics as an adjunct to systematic specific causation in forensic medicine. *Wien Med Wochenschr* 2011;**161**(2).
22. Kohles SS, Freeman MD. Mathematical models characterizing the probability of trigger event, ambient-risk, and coincidental influences on inductive and abductive conclusions of specific causation. *Ann Epidemiol* 2010;**20**(9):713–4.
23. Zhang S. Pivotal steps towards quantification of molecular diffusion coefficients by NMR. *ChemPhysChem* 2007;**8**(5):635–42.
24. Afari N, Harder LH, Madra NJ, Heppner PS, Moeller-Bertram T, King C, Baker DG. PTSD, combat injury, and headache in Veterans Returning from Iraq/Afghanistan. *Headache* 2009;**49**(9):1267–76.