A brief literature survey into the effects of coal seam gas exploration by-products on Human EEG

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Abstract

Environmental toxins are rapidly increasing as more new chemicals are synthesised and applied in agriculture, nutrition and industry including conventional and unconventional mining exploration. In the coal seam gas (CSG) exploration industry, fracking or fracturing and venting are common methods of extraction where several hundred known and unknown chemicals are used or released from the ground during the mining and venting process. Chemicals associated with fracking can lead to headaches and migraine, stress and anxiety, toxic encephalopathy as well as dizziness/balance problems and seizures. Quick and accurate as well as economical diagnostic tools are required for confirming neurological disease or toxic encephalopathy. Quantitative electroencephalography (qEEG) is one such tool for obtaining baseline data that may be associated with toxic encephalopathy. Characteristic EEG findings from the literature are focal or generalised slowing in the delta and theta frequencies or fast beta rhythms indicative of diffuse or focal cerebral structural damage and dysfunction. This paper discusses some of the common chemicals associated with CSG mining and associated EEG findings.

Keywords: Encephalopathy; Coal Seam Gas, toxins; Electroencephalogram

ARTICLE INFO	
RECEIVED	September 18, 2019
REVIEWED	October 24, 2019
ACCEPTED	February 23, 2020

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1. Introduction

The Environmental Protection Agency of the United States of America reported the use of 84,000 chemicals by 2012, which does not include chemicals produced in low volumes. The number of new chemicals added each year is approximately 1,000 to 2,000. Ensuring public health has become increasingly difficult despite improvements in large scale monitoring, better awareness of health risks and increased human relevance associated with the increase of chemicals into the environment (Pool & Rusch, 2014). Neurological problems such as headaches, dizziness, disorientation, depression and encephalopathy have been associated with products listed by coal seam gas mining (CSG) companies. Characteristic, although not specific EEG changes have also been reported following exposure to products associated with coal CSG mining such as chemicals and heavy metal particulate matter, which may be signs of toxic encephalopathy.

2. Encephalopathy

Encephalopathy is defined by nonfocal or symmetrical brain dysfunction caused by histopathological changes, in the cortical and subcortical areas of the brain but is in many cases asymptomatic depending on level and length of exposure (Kim & Kim, 2012). Encephalopathy is associated with altered mental states, memory loss, cognitive decline, and personality changes, lack of concentration and attention and lethargy. There are many causes of encephalopathy including bacteria, viruses, solvents, drugs, radiation, paints, industrial chemicals, and some metals as well as metabolic or mitochondrial dysfunction. The most common encephalopathy discussed in the literature is metabolic encephalopathy, which is characterised by systemic organ dysfunction including the liver and kidney leading to increased toxic metabolites and cerebral histopathology (Perugula & Lippmann, 2016).

The National Institute of Neurological Disorders and Stroke listed 836 clinical trials related to encephalopathy in 2019 with one trial addressing carbon monoxide poisoning, 138 for hepatic encephalopathy, seven mitochondrial encephalopathy studies, seven sepsis-related encephalopathy studies, 26 substance-related disorders of which two addressed hepatic encephalopathy and 17 listed as toxaemia, which included five associated with septic encephalopathy (Clinical Trials). No clinical trials on toxic encephalopathy or environmental encephalopathy were listed. However continuous exposure to various environmental, industrial, nutritional and/or agricultural toxins is increasing and can lead to peripheral or central nervous system dysfunction and hallmarks of toxic encephalopathy. Examples of toxic encephalopathy with possible encephalogram anomalies include spastic paraparesis caused by β-N-methylamino-Lalanine (BMAA) in lathyrus sativus peas, exachloraphene encephalopathy, mercury encephalopathy, acute ethylene glycol poisoning and organic solvent encephalopathy (Dobbs, 2011; Valk & van der Knaap, 1992). A closer look at signs and symptoms of possible neurotoxicity that may show EEG anomalies include severe fatigue, weakness, headaches, spontaneous nose bleeds, numbness and paraesthesia, twitching or unusual movements, clumsiness or unsteadiness (McCarron, 2013).

2.1 Toxic encephalopathy diagnostics

Toxic encephalopathy may be an outcome of exposure to environmental toxins. Both physical and neurological examination is required to establish the presence of toxic encephalopathy. Diagnosis of toxic encephalopathy can be divided into acute diffuse toxic encephalopathy or chronic toxic encephalopathy. To date only a limited number of physical signs have been identified that are associated with specific environmental toxins and include blue gums following lead intoxication (Rao, Vengamma, Naveen, & Naveen, 2014). Acute diffuse toxic encephalopathy is relatively easy to identify as there is a distinct correlation of symptoms with time since exposure and place of exposure to a known toxin. Acute diffuse toxic encephalopathy is characterised by mild euphoria, stupor or seizures, which can lead to coma and death. Chronic toxic encephalopathy involves continuing diffuse injury to the brain resulting from cumulative or repeated exposures over months or years to solvents or heavy metals and involves varying degrees of impairment (Firestone & Longstrength, 2004). Chronic toxic encephalopathy is more difficult to diagnose and consists of a number of subcategories depending on severity and length of exposure. Chronic toxic encephalopathy manifests as mood disorders, deficits in attention, memory and learning as well as decreased psychomotor function. Cerebellar syndromes include gait ataxia, dysarthria, intension tremor, gaze-evoked nystagmus, most often due to methyl mercury, methyl bromide, dimethyl and trimethyl compounds. Manganese and carbon disulphide can lead to Parkinsonism and vascular encephalopathy respectively (Kim & Kim, 2012). Encephalogram (EEG) changes associated with encephalopathies are similar, whether due to septic, metabolic, toxic, or structural causes. Non-invasive and simple EEG analysis may provide some indication of structural changes due to encephalopathy including toxic encephalopathy.

2.2 EEG findings

Assessment of EEG rhythm characteristics provides information on focal or lateralised abnormalities of the brain, which could suggest a structural basis for an encephalopathy if the intermittent or persistent focal slowing is observed consistently and hence corresponds to a focal or generalized cerebral dysfunction or both (Andraus & Alves-Leon, 2011). EEG records associated with drug or toxin encephalopathy can show focal or generalised slowing in the delta and theta frequencies indicative of diffuse or focal cerebral dysfunction, or fast beta rhythms (Smith, 2005). However, in more severe encephalopathy cases burst-suppression, background suppression and cerebral electrical inactivity can also be present. In addition less common patterns include alpha coma, spindle coma and triphasic waves (Altwegg-Boussac et al., 2017).

3. Chemical Use in Coal Seam Gas Exploration

The number of chemicals used in CSG mining, fracking and venting is estimated to be approximately 1,000. An investigation by the United States Committee of Energy and Commerce in 2011 published results from a survey of 14 oil and gas service companies about types and volumes of hydraulic fracturing products used between 2005 and 2009 (Kim & Kim, 2012). Results indicated the use of more than 2,500 products containing 750 chemicals and other components. Although some were harmless to health, others that are hazardous to health included benzene and lead and for many exposure to these is occurring daily in non-CSG mining areas such as petrol stations. Twenty nine of the 750 chemicals and components are known to be possible human carcinogens and were contained included in the list of the 2,500 products. BTEX compounds – benzene, toluene, ethylbenzene and xylene were part of 60 hydraulic fracturing products (Waxman, Markey & DeGette, 2011). Most chemicals used in CSG mining are either not disclosed or not been assessed for toxicity and short or long term health effects. In the USA between 2005 and 2009 the 14 companies investigated reported using 94 million gallons of 279 products that contained at least one product that was undisclosed (Waxman, et al., 2011). Disclosure of chemicals used in mining and fracking is not required in Australia or in the United States of America. A Bill passed by the American Government in 2005 which exempts fluids used in the natural gas extraction process of hydraulic fracturing from protection under the Clean Air Act, Clean Water Act and Safe Drinking Water Act and from regulation by the Environmental Protection Agency is referred to as the Haliburton Loophole (Palmer, Short & Auch, 2018). However, approximately 40-50% of chemicals used during CSG mining could affect the brain or nervous system, of which some at concentrations below current recommended as hazardous (Colborn , Kwiatkowski , Schultz & Bachran, 2001). An example of what has been proclaimed as clean energy and hence not hazardous by the CSG Industry is the emissions of the Curtis liquefied natural gas plant which released 4,800 tonnes of carbon monoxide, 4,300 tonnes of nitrous oxides, 620 tonnes of volatile organic compounds and 190 tonnes of carcinogenic formaldehyde (Lloyd-Smith & Senjen, 2011). A report compiled by Wayne Somerville (Somerville, 2014) lists some of the chemicals in use for CSG mining in Australia (Table 1).

Table 1. Known chemical used in CSG mining operations in Australia

Drilling Fluid	**Hydraulic Fracturing**	**Fracking**
Viscosifiers (bentonite, polyacrylamide)	Gelling agents (guar gum, diesel, alkanes/alkenes)	Corrosion inhibitors (e.g., formamide, methanol, naphthalene, naptha, nonyl phenols, acetaldhyde)
Weighting agents (barium sulphate)	Gel stabilisers (sodium thiosulphate)	Scale inhibitors (e.g., ethylene glycols)
Bactericides/biocides (glutaraldehyde)	Gel breakers (Ammonium persulfate, sodium persulfate)	Iron control agents (e.g., citric acid, thioglycolic acid)
Salts (KCl, NaCl, $CaCl_2$)	Friction reducers (polyacrylamide, mixtures of methanol, ethylene glycol)	pH adjusting agents (sodium or potassium carbonate)
Breakers (diammonium peroxydisulphate, hemicellulase enzyme)	Surfactants (isopropanol, 2-Butoxyethanol /2-BE)	Diluted acid to dissolve minerals (e.g., hydrochloric acid, muriatic acid)
Scale inhibitors (anionic polyacrylamide, acrylamide copolymer)	Biocides (glutaraldehyde, Tetrakis hydoxymethyl phosphonium sulfate/THPS, 2-Bromo-2-nitro-1,3-propanediol (Bronopol), 2,2-Dibromo-3-nitrilopropionamide	
Emulsifiers and deemulsifiers	Clay stabilisers (tetramethyl ammonium chloride)	
Polymer stabilisers (Sodium sulfite)	Buffer fluids and cross-linking agents	
Defoamers (glycol blends, light aromatic and aliphatic oil, naptha)		
Corrosion inhibitors (zinc carbonate, sodium polyacrylate)		
Lubricants (chlorinated paraffins)		

The National Toxins Network in Australia reported that of the 23 compounds it has identified as toxic, only two have been assessed by the National Industrial Chemical Notification and Assessment Scheme (NICNAS) (Lloyd-Smith & Senjen, 2011) despite glutaraldehyde, brominated biocides, propargyl alcohol, 2-butoxyethanol and heavy naphtha having been found to be dangerous at concentrations near or below chemical detection limits (Somerville, 2014). Additional substances known and reported to be associated with CSG mining are shown in Table 2.

Table 2. Additional CSG Chemicals

2-methyl phenol	Chloride	Silver
Acrylamide polymer	Copper	Styrene
Arsenic	Cyanide	Uranium
Barium	HMX (Octogen)	Diesel
Benzene, Toluene, Ethylbenzene, Xylene (BTEX)	Methane	Radon
Cadmium	Poly-aromatic hydrocarbons	

Only a limited number of these compounds have been assessed for their neurological effect using any available modality such as MRI, PET or EEG.

3.1 CSG chemicals and EEG findings

Organic solvents and other substances containing toluene associated with CSG exploration are known to cause multifocal neurologic pathology and mental disorders, cerebral, cerebellar and brain stem atrophy, and diffuse focal white matter abnormalities detectable by MRI and EEG changes in animals and humans (Takeuchi & Hisanaga, 1977; Valk & van der Knaap, 1992). A closer look at some of these and other compounds associated with CSG exploration follows.

3.2 Carbon dioxide and radioactive emissions

Atmospheric enrichment of carbon dioxide and radon-222 gas has been reported in the Tara coal seam gas fields in Australia (Tait, Santos, Maher, Cyronak & Davis, 2013). Increased carbon dioxide leading to blood alkalosis can interfere with cerebral function by a relative increase in low frequency power in the delta (1-3 Hz), theta (4 to 7 Hz) and alpha (8-13 Hz) range of the quantitative EEG (qEEG) spectra indicating reduced brain arousal (Kety & Schmidt, 1946; Posner & Plum, 1960; Xu et al., 2011). Default mode network investigation has also indicated a significant reduction between normocapnia and hypercapnia in the connection between the posterior cingulate cortex, bilateral inferior parietal regions, medial prefrontal cortex, and medial temporal lobe. With similar results in the sensory motor networks of the brain using fcMRI (Xu et al., 2011). Radon-222 (radon) has been studied extensively as an environmental toxin and has been shown to be associated with lung cancer. However, radon gas may also affect different parts of the brain with different areas having different susceptibility to radon gas. The amygdala and hippocampus being the most susceptible with the proviso that susceptibility differs between individuals. What increases susceptibility is not known and hence setting threshold values may not prevent radon-caused toxic encephalopathy (Momčilović, Lykken & Cooley, 2006). However, radiation therapy, which has a different dose exposure to possible radon emissions from CSG mining has led to leukoencephalopathy in some patients with EEGs characterised by diffuse background slowing consistent with moderate to severe toxic encephalopathy and no focal or epileptiform waveforms (Cummings et al., 2016). No publications were found discussing EEG findings associated with increased environmental cesium-137 or lead-210, two substances also found in areas of CSG exploration.

3.3 Lead and cadmium

Lead poisoning is one of the earliest reported occupational diseases known and already common in Ancient Greece and the Roman Empire (Woolley, 1984). Lead and cadmium effects on sensory evoked potentials and qEEG have been reported from the early 1980tees (Benignus, Otto, Muller, & Seiple, 1981; Otto, Benignus, Muller & Barton, 1981; Thatcher & Lester, 1985). Thatcher and co-workers reported an increase in the amount of slow wave activity in the EEG and a decrease in the amplitude of the EEG. To note is that lead and cadmium have different affinities for cortical and subcortical regions and susceptibility to altered CNS function and convulsion varies with age and exposure levels (Thatcher, McAlaster, Lester, & Cantor, 1984). Examination of qEEG z-scores reported by Cantor showed one third of cases with anomalous findings in the frontal regions with increased θ-band relative power and abnormal hypercoherences (Cantor, 2000). Alpha and β activities of the EEG may also be more abundant in long term exposure to lead (Kovala et al., 1997). Mani et al. (1998) however did not observe any EEG anomalies in their cohort. Quantitative EEG findings included δ- and θ-band amplitude that decreased with age. Scalp sensor location at P3 and P4 indicated a greater amplitude at P3, and bilateral communality increased with age in the δ-band. These EEG changes were observed with low level lead exposure without any clinical or behavioural symptoms present (Benignus, et al., 1981). A more recent case study using MRI reported bilateral symmetric anomalies of the thalamus, lentiform nucleus, external capsules, and sub-cortical white matter suggesting toxic demyelination (Rao, et al., 2014). Cerebellar white matter and demyelinating peripheral neuropathy have also been reported with lead poisoning and seizures may also be present due to inhibition of gamma-aminobutyric acid (GABA) transmission (Landrigan & Todd, 1994; Mani, Chaudhary, Kanjalkar & Shah, 1998; Silbergeld, Miller, Kennedy & Eng, 1979)

3.4 Nitrous Oxide

Nitrous oxide is a NMDA receptor antagonist and used clinically for sedation and possibly for depression. Nitrogen oxides are generally non-toxic at low concentrations, and are a by-product when CSG is treated for sale. Nitrous oxide emissions have risen from 710 tonnes in 2013-14, to 1,300 tonnes in 2014-15 (McCarron, 2013). Neurological assessment has shown a dose-dependent reduction in P-300 amplitude and prolongation of P-300 latency of evoked potentials when psychomotor impairment was present following an acute dose of nitrous oxide. However, these changes in brain function were not apparent with EEG suggesting that measures of evoked potential are possibly more sensitive compared to EEG (Estrin, Moore, Letz & Wasch, 1988). In another study five increasing concentrations of nitric oxide were investigated and administered for 15 min. EEG was recorded bilaterally at the frontal poles. At the highest concentration the EEG showed increased θ-band, β at the 40-50 Hz, and 70-110 Hz band powers (Rampil, Kim, Lenhardt, Negishi & Sessler, 1998). Emerging slow wave rebound activity may also be present once nitrous oxide is withdrawn.

3.4 BTEX in coal seam gas mining

BTEX which stands for benzene, toluene, ethylbenzene and xylenes is a Volatile Organic Compounds (VOR) found in tar, crude petroleum, diesel and petrol fuels and a variety of petroleum-related products and used by the CSG industry as a solvent. Naturally occurring BTEX compounds are typically found in seawater around areas of natural gas and petroleum deposits, coal

deposits and in gas emissions from volcanoes and bushfires. BTEX has been banned by both the NSW and Queensland Governments for use in CSG mining however due to naturally occurring BTEX found in soil and released in the flowback water, ground water contamination can still occur and become a health hazard (Waxman et al., 2011; Webb et al., 2018).

Solvent toxicity generally manifests as diffuse or localised θ-band activity. Reported prevalence of EEG anomalies associated with industrial solvents including benzene ranged between 35% to 80% (Seppäläinen, 1988). No specific data was located for effects of benzene on EEG. EEG findings associated with ethylbenzene are most often generalised with paroxysmal changes (Indulski, Sińczuk-Walczak, Szymczak & Wesołowski, 1996).

Toluene toxicity has been reported in several studies with concomitant EEG findings. Toluene leukoencephalopathy is the main neuropathology associated with white matter damage. Other neuro- and psychopathology includes ataxia, tremors, emotional lability and mental changes (Filley, Halliday & Kleinschmidt-Demasters, 2004; Satran & Dodson, 1963). An animal model of toluene exposure indicated that EEG characteristics vary with toluene concentration and with sleep-wake cycle as well as with respect to CNS location. In a study comparing the highest exposure group to the lowest indicated that for the highest toluene concentration δ_1 diminished and β_1 and β_2 cortical components increased significantly. In contrast in the lowest toluene exposure group, δ_1, θ, and α bands were significantly reduced but β_1 and β_2 bands showed no significant change (Takeuchi & Hisanaga, 1977).

Xylene is generally considered to be more acutely toxic than benzene, but similar to toluene (Bergman, 1979). Acute effects of solvents including xylene on the central nervous system can be observed already at very low concentrations (Gamberale, Annwall & Hultengren, 1978). Xylene can lead to giddiness, anorexia, and vomiting and exacerbate seizures in susceptible individuals. Occupational exposure to xylene has been associated with anaemia, thrombocytopenia, leukopenia, chest pain with ECG abnormalities, dyspnoea and cyanosis, in addition to CNS symptoms (Langman, 1994). Exposure may increase the dominant α-band frequency and percentage. However, the effects of short-term xylene exposure on EEG were minor, and no deleterious effects were noted (Seppäläinen et al., 1991).

3.4 Carbon monoxide

Carbon monoxide is emitted during flaring and from machinery. Acute carbon monoxide poisoning can lead to lateralized sharp waves and a focal electrographic seizure discharge within hours of the exposure as well as delayed toxic encephalopathy and cognitive sequelae. MRI imaging found bilateral abnormal white matter changes within the cerebral hemispheres and abnormal signal intensity within the basal ganglia putamen and caudate nuclei (Neufeld, Swanson & Klass, 1981; Tapeantong & Poungvarin, 2009). No EEG reports associated with carbon monoxide were found.

3.5 Sulfur dioxide and hydrogen sulfide

Hydrogen sulfide occurs naturally in some gas formations and can be released when gas is vented or flared, or via fugitive emissions. Hydrogen sulfide, is a potent neurotoxin. Sulfur dioxide and hydrogen sulphide are components of coal seam gas but are also produced by diesel equipment (Esen, Özer, Soylu, Rend & Fisne, 2018). These gases lead to oxidative stress and neurotoxicity (Zhang, Vincent, Halliwell, & Wong, 2004). Exposure to sulfur dioxide and hydrogen sulphide can lead to decreased mitochondrial DNA and loss of ATP, which may have an effect seen by EEG as a consequence of energy failure and toxic encephalopathy (Tzoulis et al., 2010). Hence increased δ-band activity may be assumed in response to loss of ATP to conserve energy (Dworak, McCarley, Kim & Basheer, 2011).

3.6 VOCs, formaldehyde, glutaraldehyde and styrene

Volatile organic compounds (VOC) contain benzene and ethyl-benzene, which have adverse neurologic and respiratory effects. Formaldehyde forms when methane is exposed to sunlight and then transforms to carbon dioxide by photo-oxidation in ambient air (Kaden, Mandin, Nielsen, & Wolkoff, 2010). Formaldehyde, naphthalene and benzyl chloride were reported to be used in 34% of all hydraulic fracking operations in the United States between 2010 and 2011 (https://www.ecowatch.com/2013/cancer-causing-chemicals-fracking-operations/). Increased formaldehyde around CSG fracking sites is also due to truck traffic and as a biocide to prevent biodegradation of organic additives in CSG mining (Lloyd-Smith & Senjen, 2016; Sorg, Tschirgi, Swindell, Chen & Fang, 2001). Formaldehyde may lead to thirst, headaches, dizziness, apathy, and inability to concentrate. The effect of formaldehyde on EEG is unclear with studies reporting a dose-dependency but in some instances no EEG changes have been observed (Fel'dman & Bonashevskaya, 1971; NRC, 1980).

Sarin is a nerve gas and belongs to the group of VOCs, which has been extensively studied and EEG analysis reported. EEG analysis to sarin exposure, indicated long-term effects on EEG. Statistically significant effects of sarin were marked desynchronised EEG with increased β-band activity, increased δ and θ band slowing, and decreased α-band activity. At higher doses, VOCs may lead to convulsions and muscular paralysis, characterised by a general slowing of the EEG and spike wave discharges (Duffy, Burchfiel, Bartels, Gaon & Sim, 1979). VOCs share similar structures and pharmacological action and therefore this study may be extrapolated to VOCs associated with CSG mining and venting.

Glutaraldehyde has similar properties to formaldehyde and is also used as a biocide by the CSG industry. It is present in produced water as part of the fracking operation (Campa et al., 2018). A suspected case of glutaraldehyde poisoning was reported in 2002 with headache, loss of attention, dizziness, anxiety, drowsiness and alteration of homeostatic reflexes (Proietti, Longo & Duscio, 2002). No specific reports discussing the toxic effects of glutaraldehyde on EEG were located in the current study. Glutaraldehyde however has led to a significant increase in deaths due to leukaemia, and brain, colon and prostate cancers in a group

of embalmers, anatomists and pathologists compared to an age controlled group (van Birgelen et al., 2000). Glutaraldehyde may also lead to mitochondrial dysfunction and ATP depletion and therefore may cause similar changes to the EEG as discussed above for sulfur dioxide (Lin, Yuan, Deng, Niu & Chen, 2019; Tiffert, Garcia-Sancho & Lew, 1984).

Abnormal EEG were found in 24% of participants in a study of styrene exposure reported by Seppäläinen (Seppäläinen, 1988). EEG anomalies included were excessive diffuse θ-band activity and localized slow waves in the posterior regions. Bilateral spike and wave (S&W) discharges may be present as well as focal slow wave activity. Continuous exposure to VOCs may also lead to environmental chemical odour intolerance or chemical sensitivity, which has a different presentation to environmental toxin exposure (Miller, 2001). Common signs and symptoms may include decreased REM percent and longer REM onset latency (Bell et al., 1996).

3.7 Diesel

Diesel exhaust is a mixture of combustion derived nanoparticles (CDNP) and hydrocarbons, carbon monoxide, nitrous oxides, polycyclic aromatic hydrocarbons (PAHs) and redox metals (Crüts, et al., 2008).

Particulate matter in the nanoparticle range such as found in exhaust diesel can translocate into the brain via the olfactory nerves leading to extensive oxidative stress (Oberdorster, et al., 2004). Carbon monoxide, nitrous oxides and hydrocarbons may also lead to decreased θ and α, and increased β and γ-band EEG changes via vagal reflexes from the lungs (Koo, 2001; Lewine, Paulson, Bangera, & Simon, 2019; McQueen et al., 2007). A recent study of exposing volunteers to dilute diesel exhaust as a model for ambient particulate matter exposure indicated a significant increase primarily in the β_2 power frequency (20-32 Hz) in the frontal cortex at Fp1 and Fp2 and F3, F4 following 30 minutes of exposure. Median power frequency changes spread to central C3 and C4 as well as to parietal sites, P3 and P4 but no significant change in β_2 power was observed. β1 activity (15–20 Hz) also increased during diesel exposure at the frontal cortex, but was not significant, whilst no significant change was observed for δ, θ and α-bands when compared to the sham group. The findings suggested increased left frontal cortex activity (Crüts et al., 2008).

Many more chemicals and particulate matter have been investigated and found to have toxic effects. Of those in public lists, not all are known to lead EEG anomalies. For a list of these the reader is referred to the various Government publications and also for a comprehensive list by Geralyn McCarron and the publications by Mariann Lloyd-Smith (Lloyd-Smith & Senjen, 2011, 2016; McCarron, 2013). Further research is therefore required to establish biomarkers for substances associated with Coal Seam Gas mining and venting and their association with neuropathology and EEG findings. Table 3 provides an overview of location and effects of some of the main chemicals associated with fracking but is not exhaustive as more research is required for many of the chemicals listed and those mentioned in the tables above.

Table 3. Local, EEG characteristics and neurology associated with known fracking chemicals.

Chemical	Location	EEG Characteristic	Neuropathology
Organic solvents	Multiple sites		Multifocal neuropathology Mental disorders CNS atrophy
Carbon Dioxide	posterior cingulate cortex, bilateral inferior parietal regions, medial prefrontal cortex, and medial temporal lobe	Increase in low frequency power	Reduced brain arousal
Radon-222	Amygdala, hippocampus, temporal lobe, frontal lobe, occipital lobe, parietal lobe, substantia nigra, locus ceruleus, nucleus basalis	Possible diffuse background slowing	Alzheimer's disease
Cesium-137	No publications		
Lead & Cadmium	Frontal regions P3 and P4 Thalamus, lentiform nucleus, external capsules, and sub-cortical white matter. Cerebellar white matter	Increase slow wave activity and decrease in EEG amplitude Hypercoherence Increased θ-band relative power in posterior areas More α and β activities	Seizures, irritability, headache, mental dullness and attention difficulty, memory loss, tremor, and hallucinations
Nitrous Oxide	Frontal areas	Increased θ-band, β at the 40-50 Hz, and 70-110 Hz band powers	Atrophy, changes in corpus callosum, Extensive white matter change in both hemispheres
BTEX		δ_1, β_1 and β_2, θ, and α bands	giddiness
Carbon Monoxide	Lateralised sharp waves, Bilateral white matter change	No changes in EEG reported	Focal seizures
Sulfur Dioxide & hydrogen Sulfide	hippocampus	Increased δ-band and Θ-band activity	motor, behavioural, and cognitive deficits dementia
Formaldehyde & Glutaraldehyde	unclear	Possible increased δ-band and Θ-band activity with glutaraldehyde	headaches, dizziness, apathy, and inability to concentrate
Sarin	General slowing of EEG	desynchronised EEG with increased β-band activity, increased δ and θ band slowing, and decreased α-band activity	convulsions and muscular paralysis

Styrene	Posterior regions	excessive diffuse θ-band activity and localized slow waves; Bilateral spike and wave discharges; Focal slow wave activity	decreased REM percent and longer REM onset latency
Diesel	Fp1 and Fp2 and F3, F4 C3 and C4 P3 and P4	decreased θ and α, and increased β and γ-band EEG changes via vagal reflexes from the lungs	Alzheimer's disease

4. Prevention and Treatment Options for Toxic Encephalopathy

Foremost is the removal of the toxic substance from the environment or in most instances removing the person from the source of the toxin. Regular detoxing by workers exposed to fracking may reduce exposure caused neuropathy. Toxic encephalopathy needs to be carefully investigated as it may be asymptomatic or signs and symptoms of toxin exposure may have a similar presentation to psychiatric signs and symptoms, metabolic, inflammatory, carcinogenic and neuropathological signs of diverse etiology (Schaumburg & Spencer, 1987). Therefore, it is essential to have an accurate occupational history and detailed neurological examination result. Treatment is then based on the extent of the signs and symptoms displayed by the patient and the toxic substance causing the neuropathology (Berisavac et al., 2017).

Prevention should be considered in all cases by reducing exposure to toxins and providing sufficient safeguards such as protective clothing. Neurofeedback is an adjunct or alternative therapy often found efficacious for epilepsy, anxiety and psychosis often associated with toxic encephalopathy. Neurofeedback treatment protocols focus on training alpha, beta, delta, theta, and gamma or a combination of these. Alternative modes include amplitude training or z-score training amongst others. The observation that seizure incidence due to inhalation of lunar landing fuel by NASA astronauts was lowered significantly by sensory-motor rhythm neurofeedback training (Sterman & Egner, 2006) suggests that neurofeedback may be useful in normalising EEG rhythm patterns or reducing the incidence of toxic encephalopathy in toxin exposed workers by enhancing neuronal or brain reserve by enhancing the capacity to compensate for dysfunction. However, caution needs to be exercised when providing neurofeedback as an incorrect protocol may result in an increased blood flow to the brain and hence increase the toxic effects of the chemicals. This application of preventative neurofeedback requires further research to address the increasing use of industrial chemicals.

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