Neurotoxic Environmental Exposures to PCB’s in Neurological Disease Onset

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**Introduction**

Polychlorinated biphenyls (PCB’s) are organic chemical compound mixtures synthesized by man and valued for its ability to insulate products while resistant to burning from high temperatures. The unique properties of PCBs made them ideal for widespread industrial and commercial applications. Thus, they were convenient additions for plastics, electrical appliances, capacitors, insulators, and oil lubricants for engines for 50 years commercially. However, growing evidence supporting toxicity health hazards upon exposed individuals became more apparent over time. The danger to both human and environmental health from exposure to PCBs effectively led to their disbandment of production in the United States by the Environmental Protection Agency (EPA) in the year 1977. However, discontinuation of PCB’s does not eliminate possible exposure to the public today. The slow degradation and persistence from high boiling points still expose many individuals to harmful health effects from PCB’s and degradation products from waste incineration. PCB trace amounts in the environment are common in water, aerial, and sediment samples collected; furthermore, bioaccumulation across the food chain in animals consumed by humans. Certain groups within human populations are more susceptible to severe health ramifications resulting from PCB exposures; particularly, individuals exposed to these chemicals during critical developmental stages in life such as the perinatal stage in the mother’s womb. The evidence on PCBs neural toxicity directly being responsible for neurological disorders is lacking due to complex variables. However, the associative potential of PCB exposures contributing largely to neurodegenerative disease risk for Alzheimer’s Disease, Parkinson’s Disease, and various cognitive attention disorders is a definitely plausible. Epidemiologic studies in large part have affirmed multiple neurological disorders following environmental exposure to PCBs at low trace levels in population human studies. Several animal-based disease models for PCB trace amounts of have also provided evidence support neurological junction critical to neurological development during a lifetime have yielded results of physiological and social detriments to neurocognitive functioning. However, policy makers must still access confounding variables from extrapolation of animal model validity to consideration; meanwhile, discern if other factors play a more attributable factor to human neurodegenerative dysfunction rather than PCBs. There is a raised hazard in neurological development at the prenatal or gestational susceptible period in life where adverse effects from exposures to PCBs may have remained latent until exposed at older age. Thus, this paper will investigate if early life exposure from prior to the banning of products that used PCB’s in aged adults may have a role in the increased trend of neurodegenerative diseases in the US. The purpose of this paper is to provide a scientific review that serves to illuminate a deeper mechanistic understanding on how PCB’s primarily alter proper neurological system functioning through exposure to these agents at earlier critical developmental stages in their lifetimes and to see if the rising trend pattern of neurodegenerative diseases affecting adults in the US may be a result of PCB exposure consequences.

**Population-based Studies for Neurological Diseases & PCB Exposures**

The difficulty of ascertaining a relative value for PCBs in biological samples for human populations across the United States is due to the inability to collect these samples and geographic variances in PCBs. A significant percentage of individuals who are at ages where neurodegenerative disease symptoms first begin to gradually worsen mental faculties have PCBs in their blood. In fact, PCBs are reported to be detectable in the blood of approximately 80% of Americans over the age of 50 a result of the pervasiveness of these environmental resistant chemicals (NCHS, 2016). A survey conducted by the National Center for Health Statistics using a population sample representation of over 1,200 female subjects modeling the total United States females able to bear children collected serum samples biannually in each subject approximating for a national level of multiple PCBs in blood samples at 30.1 ng/g (NCHS, 2016). The presence of PCB’s evidenced by the study in a significant portion of females that reproduce offspring transmitted these toxic elements illustrates the complexity of understanding the adverse neurological effects which may stem from inherent exposure from one’s mother. The risk of neurodegenerative diseases development may also have a higher gender specific impact for females as evidenced in occupational exposure studies on large cohort populations. One retrospective mortality study for neurodegenerative disease onset for 17,321 PCB-exposed workers who worked 90 days or longer at one of the few US capacitor factories developing PCB’s in the decades prior to its discontinuation experienced PCB occupational exposures estimated to be ten times larger concentrations of exposure than normal values resulted in sex-specific female increases for Parkinson’s Disease and Dementia mortality rates in follow up analysis (Steenland *et al*., 2006). The likelihood of Parkinson’s Disease in later life increases when individuals exhibit higher trace values of PCB congeners in serum samples from brain tissue. One study on post mortem brain tissue samples of Parkinson’s Disease (PD) stricken individuals with high levels of PCB congeners found in brain tissue exhibited much higher values of PCBs and Parkinson rates in female samples illustrating the susceptibility of females to PCB induced neurotoxicity (Hatcher-Martin *et al.*, 2012). One of the remaining primary exposures from persistent PCBs still present in the environment can be through the ingestion of fish or marine mammals which bioaccumulation PCBs across the food chain due to the strong persistence and runoff of PCBs into water systems. One cohort study examining individuals who consumed high amounts of whale blubber as part in their diets corresponded to higher rates of PD in samples (Peterson et al., 2008). The strength of resistance through bioaccumulation capability of PCBs is also evidenced in the isolated Faroe island population an environment which one would be limited in material contact with PCBs yet PD is twice as prevalent in adults than compared to individuals from industrialized PCB usage (Farrell et al., 2016).

**Animal In-Vitro Models in Neurological Diseases & PCB Exposures**

Animal or in-vitro models also provide evidence for PCB induced detrimental impacts which progressively lead to neurodegeneration of healthy a neurological system. An animal study analyzing the effect of early life exposure to PCBs and its effect later in life demonstrated that early exposure to low levels of NDL-PCBs exhibited higher vulnerability to amyloid beta induced stress an important feature in Alzheimer’s Diseased individuals (Elnar et al., 2016). Further, animal in-vitro models have illustrated PCB’s ability to cross the blood brain barrier and interact with dopamine pigmented regions in the striatal part of the brain exhibiting neurotoxic features. The result of reduced pigmented dopamine neurons often are a clinical feature typical to PD afflicted individuals. The possible physiological pathway by which neurodegenerative disease loss of skeletal muscle control may be influenced by the alteration of calcium uptake channels in the sarcoplastic reticulum vital for neuromuscular motor commands. An animal study using a rabbit for a model where several PCB congeners were presented through ingestion into the internal environment of the rabbit whose tissue was then analyzed showing dysregulation in calcium channel functioning at skeletal muscle connections with neurons resulting in psychomotor and skeletal muscle abnormalities akin to PD features (Niknam et al.,2013). Furthermore, PCBs effected in several in vitro study examples as promoting calcium influx into sarcolemma cells and thyroid hormone maintenance of normal homeostasis in rat hippocampus neuron cells in multiple in vitro models.

**The Physiological Mechanisms Induced by Toxicological Response to PCB Exposure Summary**

Non-Dioxin-Like PCBs further inhibit the SOCE gene an essential component in promoting calcium signaling while GPCR mediates calcium signaling all potential mechanisms which have been evidenced in both animal and human models. Can PCBs currently exhibit similar neurotoxic alterations in these essential calcium transport channels for humans with neurodegenerative diseases more validity of animal model findings must be determined prior to ultimately defining neurotoxicity as a given outcome leading to various neurological dysfunctions more is yet to be answered] The physiological and neuronal system mechanisms induced by toxicological response to PCB exposure lead too neurodegenerative processes in the progression seen gradually over time in these neurological disorders. Can PCBs currently exhibit similar neurotoxic alterations in these essential calcium transport channels for humans with neurodegenerative diseases more validity of animal model findings must be determined prior to ultimately defining neurotoxicity as a given outcome leading to various neurological dysfunction.

**Establishment of PCB’s Health Policy Regulations**

Risk assessment of certain PCB level exposure have not been relatively easy to establish for public health officials. A large part of the difficulty can be attributed to each individual unique genetic polymorphism, metabolism, and excretion all playing a role in the toxic danger in which can be incurred from longtime PCB amounts in the body. The EPA standard for PCBs in drinking water is 0.5 parts of PCBs per billion parts (ppb) of water (EPA, 2016). Meanwhile, guidelines for water bodies which may carry remnants of PCBs which can bioaccumulate within marine animals such as tuna a common fish delicacy for humans are more tightly regulated at 0.17 ppb as a result of avoiding toxicity induced exposure on the general public from mollusks such as oysters and shellfish which have led to adverse digestive effects when contaminated by polluted PCB waterways (EPA, 2016).

**Conclusion**

PCB’s incite the onset of neurodegenerative diseases as illustrated by population models, animal & in-vitro studies, and occupational studies; furthermore, they are involved in the public health burden as illustrated by latent effects of prenatal exposure to PCB’s not yet seen and past effects in current living individuals. Future ramifications of the link between PCB’s present in higher trace amounts in women who seek to have babies should be instituted as a public health policy regulation in which they are tested for high levels of the chemicals in their bloodstream and made aware of the possible neurological risks that may be incurred to their offspring if the levels are not diminished to guideline levels not hazardous to the developing fetus. The detailed evidence presented provided evidence based neurological mechanisms of PCB’s if regulated can improve maintenance of healthy neurological functioning in animals and human being populations.

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