

Hyperbaric Oxygen Therapy (HBOT) in Young Adults with Fetal Alcohol Spectrum Disorder (FASD)

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Abstract:

A number of case reports have suggested that hyperbaric oxygen therapy (HBOT) can improve cognition and behaviors in children with Fetal Alcohol Spectrum Disorder (FASD) with documented improvement in brain blood perfusion and oxygenation. Presently it is not known whether similar favorable effects can be expected in young adults inflicted by FASD, despite more years of existing brain damage.

We describe herein dramatic and favorable effects of 100% oxygen at 1.5 atmosphere absolute in two 19 year old young women suffering from FASD with severe cognitive and behavioral deficits. The HBOT was sought by the parents after the description of the first American case, In one of these cases, a brain SPECT scan was performed and documented highly significant improvement in brain perfusion and oxygenation.

Fetal Alcohol Spectrum Behavior:

Fetal Alcohol Spectrum Disorder (FASD) describes the wide range of adverse physical, behavioural and cognitive effects resulting from ethanol exposure during embryonic and fetal development. The syndrome, described first by Lemoine in France in 1967 (1) was subsequently reaffirmed in 1973 by Jones and Smith in Seattle (2).

Understanding the mechanisms leading to FASD is critical in developing strategies for interventions. Over the last 50 years, numerous mechanisms have been proposed and tested experimentally. Goodlett and Horn have reviewed over 80 proposed mechanisms for FASD (3); however, to date very few interventional studies, either in animals or in humans have followed the mechanistic framework presented by Goodlett and Horn.

Presently children afflicted by FASD are treated symptomatically for ADHD and different forms of disruptive behavior (4).

Hyperbaric oxygen therapy for FASD

In 2005 Stoller described cognitive improvement in a 15 year old boy with FASD after undergoing 40 HBOT treatments, followed 7 months later by an

additional 33 treatments, each consisting of 60 minutes therapy of 100% oxygen at 1.5 atmosphere absolute. At a six month follow up the boy maintained his gains in verbal memory and improvement in impulsive behavior (4). The mechanisms by which HBOT might improve cognitive function in FASD have not been studied by Stoller.

Hyperbaric oxygen therapy (HBOT) is a method of delivering extra oxygen through increased air pressure (5). The FDA has approved HBOT for decompression sickness, gas embolism, carbon monoxide and cyanide poisoning, skin grafts and flaps and thermal burns (5). In recent years the medical community has been striving to examine HBOT for a variety of additional indications however the proof of effectiveness of HBOT in these indications has to await further studies (5).

Motherisk first case of HBOT for FASD in 2017 involved a 15 year old girl who was adopted at 5 months of age from a home for deserted children in the former Soviet Union (6). At the time of adoption she exhibited malnutrition and severe developmental delay. Throughout her childhood she experienced severe learning disability, attention deficit, hyperactivity and impulsivity responding well to

methylphenidate. At 14 years of age she was diagnosed with FASD, based on history of heavy maternal drinking, normal facial features and severe and complex neurocognitive and behavioral deficits.

A brain MRI, conducted prior to commencing the HBOT, showed normal anatomy. Prior to starting the HBOT, her achievements on standard neurocognitive tests showed impaired memory, attention, impulsivity, executive function and verbal performance.

After 60 plus 40 additional treatments, each consisting of 60 minutes of 100% oxygen at 1.5 atmosphere absolute , she showed marked improvement in verbal abilities (naming ability) and speed of processing information and the cognitive improvement affected daily functioning. She became able to plan her daily schedule and to better relate to people around her. She showed improved ability to read and write, both of which were very grossly delayed prior to HBOT.

Brain single proton emission computed tomographic brain imaging (SPECT) was performed prior to HBOT and after completion of the treatment series. SPECT imaging prior to HBOT showed areas of hypo- perfusion as follows: bilateral orbitofrontal, bilateral medial aspect of

temporal lobes and right dorsolateral - frontal, as well the medial aspect of the left cerebellum.

Following the two sets of HBOT treatments, there was a marked improvement in perfusion to the left cerebellum as well as the right frontal lobe. The other areas of hypo perfusion were not improved. Overall, there was an increase in the functional volume of the brain from 1126 to 1188 ml.

A follow up of the girl and her parents 2 years after completion of the HBOT revealed that the HBOT was associated with clear and sustained improvement in attention, understanding mathematical concepts, in writing comprehension of text, with less grammatical errors. The effect on impulsivity is described to have weaned off over time. There is still heightened stress and restlessness especially where she is demanded to maximize her abilities.

HBOT in 2 young adults with FASD

The question whether such changes can also be documented in adults with FASD is justified, as they have had longer periods of sustained brain insult. We describe here two cases of 19 years old females with FASD that completed HBOT in the Summer of 2019, exhibiting dramatic improvement in

brain perfusion and oxygenation demonstrated by SPECT in one of them (Figure), correlating with steep improvement in behavior, learning and social behavior. The second subject did not have a SPECT.

The first young woman suffered from learning disability, impulsivity, lack of understanding of social context and

judgement, and hyper sexuality, and lack of ability to plan or manage time or money. Following a series of 80, 1 hour hyperbaric treatments of 100% oxygen at 1.5 atmosphere absolute, there has been a marked improvement in all these domains. In parallel, there was a marked improvement in cerebral blood flow and oxygenation as documented in SPECT (Figure).

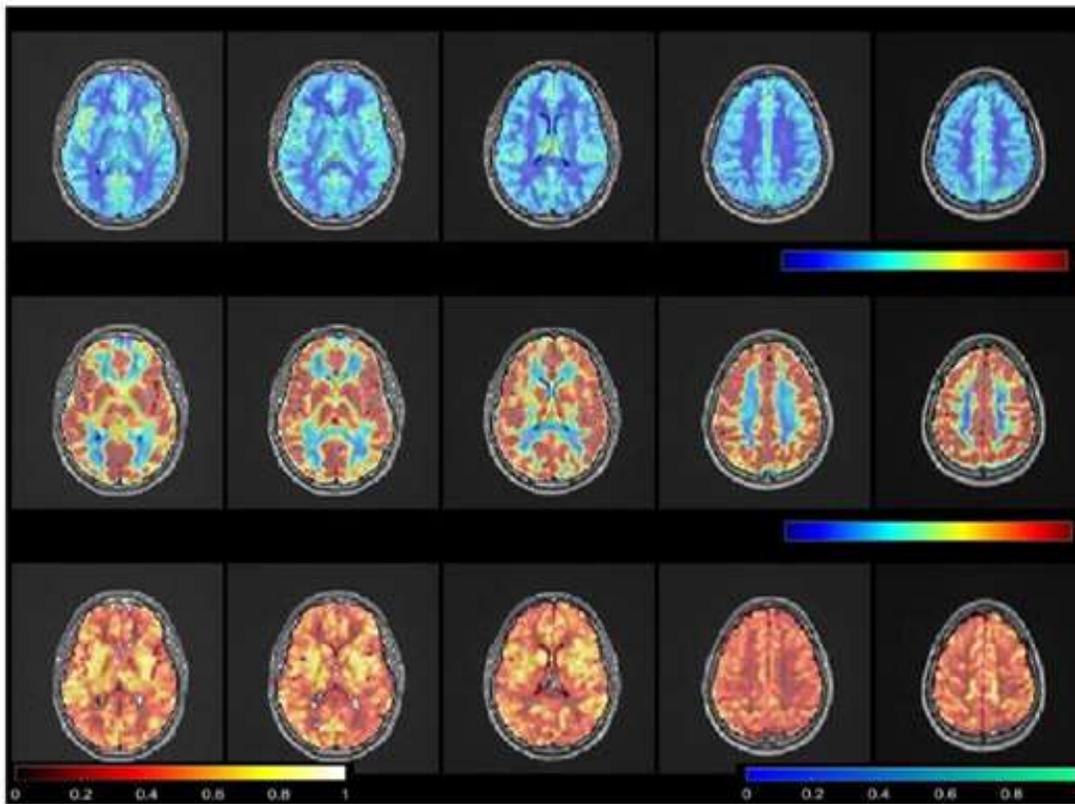


Figure: Changes in brain perfusion associated with HBOT 100% oxygen at 1.5 atmosphere absolute in a 19 yr. old young adult. SPECT Images are presented as % of maximum brain activity (upper two rows). The upper panel shows minimal perfusion, evidenced by the blue color. The second row shows much improved perfusion in red. The bottom row represents the % change in brain activity after HBOT. These changes were paralleled by steep improvement in cognitive functions and behavior.

The second 19 year old young woman with FASD suffered from attention deficit hyperactive behavior marked by extreme impulsivity and bouts of aggression leading to encounters with police and arrests. She lacked ability to plan her actions and follow up on them. Unlike the first young woman, she was treated at home by a personal hyperbaric chamber. She received 130 treatment sessions, 100% oxygen at 1.4 atmosphere absolute and first changes were noted after the first 30 treatments. Her levels of aggression decreased dramatically, her impulsivity diminished with a new ability to postpone rewards. She gained new abilities of planning her actions and executing them. Her ability to understand social circumstances improved sharply. Most importantly is a new capacity to persist in tasks she has commenced.

A Paradigm Shift in Approaching and Treating FASD

Over the last 50 years, FASD was regarded mostly as a form of static encephalopathy, where numerous neuronal functions have been permanently destroyed, explaining the inability of the brain to recuperate (4). Recent studies have provided convincing evidence that high oxygen can induce cerebral plasticity that lead to repair of

chronic impairment of brain functions. The evidence has come mostly from controlled studies in patients with traumatic brain injury and prolonged post- concussion syndrome, even when HBOT started years after the trauma (7). This is important in the case of FASD, where brain insult occurred in utero, and where one may tend to think that oxygen therapy may be too late for improvement. The documented restoration of neuronal activity in alcohol- deranged and dysfunctional brain areas indicate that that HBOT delivers to the brain sufficient oxygen to activate neuroplasticity and restore impaired function many of us assumed have ceased to exist.

Alcohol insult to different brain functions, as shown by Goodlett and Horn for FASD, can impair microvascular integrity and reduce perfusion, leading to impairment in numerous domains, including metabolism, neuronal activity, leading to loss of synapses and neuronal connectivity. The stunned areas continue to survive on anaerobic metabolism with ATP depletion, resulting in shortage of energy for healing processes. Yet, these areas can regenerate with enhanced oxygen supplementation (7).

Further research is needed to correlate the oxygenation improvement by HBOT to

Internal medicine review
Hyperbaric Oxygen Therapy (HBOT) in Young Adults with Fetal Alcohol Spectrum Disorder (FASD)
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different brain areas with the functional improvement (or lack of) to different neurobehavioral domains, in order to construct a dose-response curve to oxygen. It is quite possible that the 70-100 treatments we adopted from Stoller may not be sufficient to "lighten- up" certain areas and certain functions. This later on will be the basis for personalized HBOT for FASD.

In conclusion, HBOT shows preliminary but highly promising evidence of offering children and young adults with FASD a first ever genuine chance of improvement of their dire prognosis.

Controlled studies should be conducted in several programs worldwide to corroborate these observations.

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