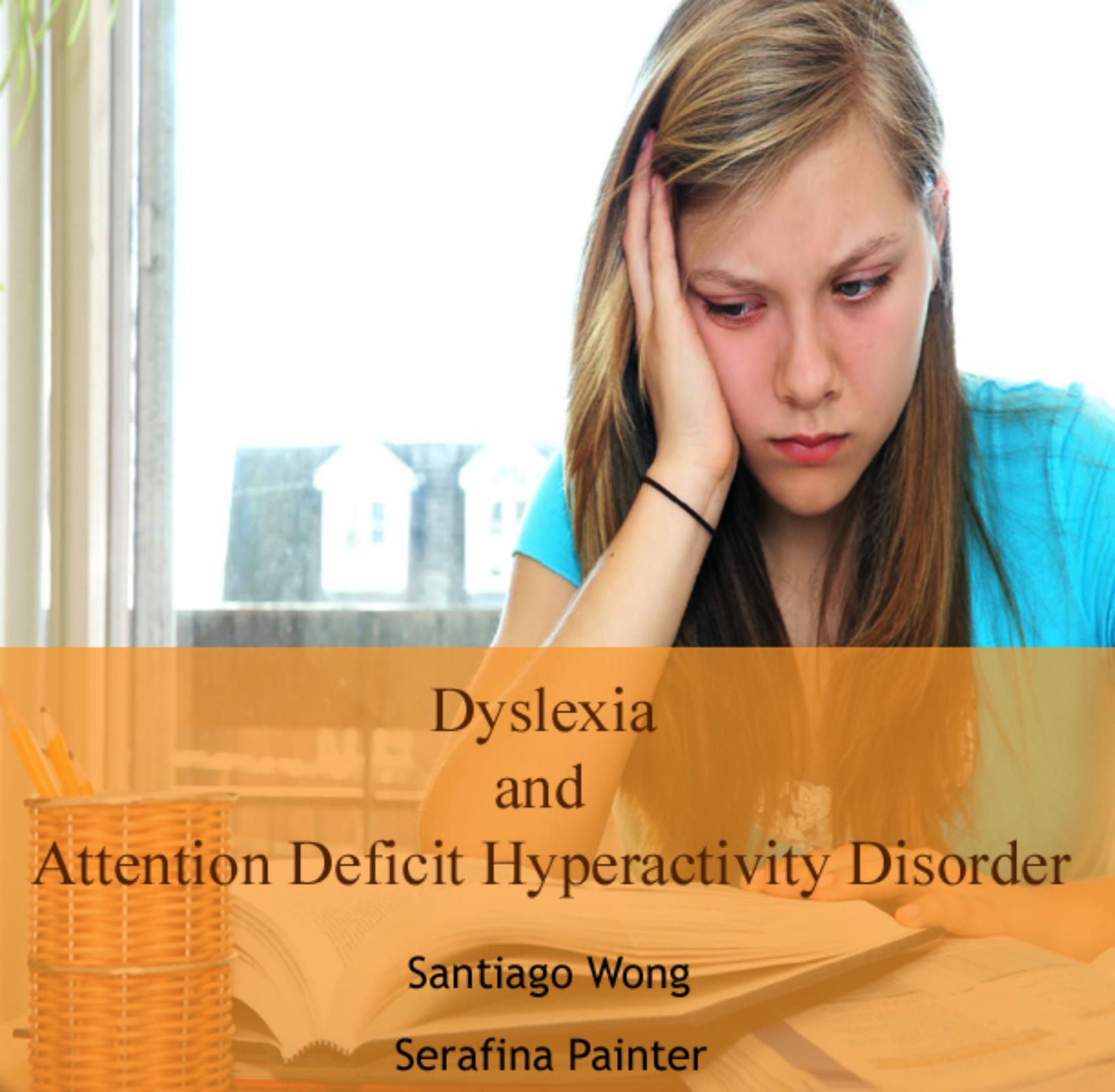

# Dyslexia and Attention Deficit Hyperactivity Disorder

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# Chapter 1

# Dyslexia

| Dyslexia | |
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**Dyslexia** is a broad term defining a learning disability that impairs a person's fluency or accuracy in being able to read, write, and spell and which can manifest itself as a difficulty with phonological awareness, phonological decoding, orthographic coding, auditory short-term memory, and/or rapid naming. Dyslexia is separate and distinct from reading difficulties resulting from other causes, such as a non-neurological deficiency with vision or hearing, or from poor or inadequate reading instruction. It is believed that dyslexia can affect between 5 to 10 percent of a given population although there have been no studies to indicate an accurate percentage.

There are three proposed cognitive subtypes of dyslexia: auditory, visual and attentional. Although dyslexia is not an intellectual disability, it is considered both a learning disability and a reading disability. Dyslexia and IQ are not interrelated, since reading and cognition develop independently in individuals who have dyslexia.

Accomplished adult dyslexics may be able to read with good comprehension, but they tend to read more slowly than non-dyslexics, and may perform more poorly at nonsense word reading (a measure of phonological awareness), and spelling.

## *Classification*

Spoken language is a universal form of man made communication. The visual notation of speech—written language—is not found in all cultures and is a recent development with regard to human evolution.

There are many definitions of dyslexia but no official consensus has been reached.

The World Federation of Neurology defines dyslexia as "a disorder manifested by difficulty in learning to read despite conventional instruction, adequate intelligence and sociocultural opportunity".

MedlinePlus and the National Institutes of Health define dyslexia as "a reading disability resulting from the inability to process graphic symbols".

The National Institute of Neurological Disorders and Stroke gives the following definition for dyslexia:

"Dyslexia is a brain-based type of learning disability that specifically impairs a person's ability to read. These individuals typically read at levels significantly lower than expected despite having normal intelligence. Although the disorder varies from person to person, common characteristics among people with dyslexia are difficulty with spelling, phonological processing (the manipulation of sounds), and/or rapid visual-verbal responding. In adults, dyslexia usually occurs after a brain injury or in the context of dementia. It can also be inherited in some families, and recent studies have identified a number of genes that may predispose an individual to developing dyslexia".

Other published definitions are purely descriptive or embody causal theories. Varying definitions are used for dyslexia from researchers and organizations around the world; it appears that this disorder encompasses a number of reading skills, deficits and difficulties with a number of causes rather than a single condition.

Castles and Coltheart describe phonological and surface types of developmental dyslexia by analogy to classical subtypes of alexia (acquired dyslexia) which are classified according to the rate of errors in reading non-words. However, the distinction between surface and phonological dyslexia has not replaced the old empirical terminology of dysphonetic versus dyseidetic types of dyslexia. The surface/phonological distinction is only descriptive, and devoid of any aetiological assumption as to the underlying brain mechanisms (Galaburda and Cestnick 2003). Studies have, however, alluded to potential differential underlying brain mechanisms in these populations given performance differences (Cestnick et al.). The dysphonetic/dyseidetic distinction refers to two different mechanisms; one that relates to a speech discrimination deficit, and another that relates to a visual perception impairment.

## *Signs and symptoms*

The symptoms of dyslexia vary according to the severity of the disorder as well as the age of the individual.

## Preschool-aged children

It is difficult to obtain a certain diagnosis of dyslexia before a child begins school, but many dyslexic individuals have a history of difficulties that began well before kindergarten. Children who exhibit these symptoms early in life have a higher likelihood of being diagnosed as dyslexic than other children. These symptoms include:

- delays in speech
- slow learning of new words
- not crawling
- difficulty in rhyming words, as in nursery rhymes
- low letter knowledge
- letter reversal or mirror writing (for example, "Я" instead of "R")

## Early primary school children

- Difficulty learning the alphabet or letters order
- Difficulty with associating sounds with the letters that represent them (sound-symbol correspondence)
- Difficulty identifying or generating rhyming words, or counting syllables in words (phonological awareness)
- Difficulty segmenting words into individual sounds, or blending sounds to make words (phonemic awareness)
- Difficulty with word retrieval or naming problems
- Difficulty learning to decode written words
- Difficulty distinguishing between similar sounds in words; mixing up sounds in polysyllabic words (auditory discrimination) (for example, "aminal" for animal, "bisghetti" for spaghetti)

## Older primary school children

- Slow or inaccurate reading (although these individuals can read to an extent).
- Very poor spelling which has been called dysorthographia (orthographic coding)
- Difficulty reading out loud, reading words in the wrong order, skipping words and sometimes saying a word similar to another word (auditory processing disorder)
- Difficulty associating individual words with their correct meanings
- Difficulty with time keeping and concept of time when doing a certain task
- Difficulty with organization skills (working memory)
- Children with dyslexia may fail to see (and occasionally to hear) similarities and differences in letters and words, may not recognize the spacing that organizes letters into separate words, and may be unable to sound out the pronunciation of an unfamiliar word (auditory processing disorder).

## Secondary school children and adults

Some people with dyslexia are able to disguise their weaknesses (even from themselves) and often do acceptably well — or better — at GCSE level (U.K. - at 16 years old). Many students reach higher education before they encounter the threshold at which they are no longer able to compensate for their learning weaknesses.

One common misconception about dyslexia is that dyslexic readers write words backwards or move letters around when reading. In fact, this only occurs in a very small population of dyslexic readers. Dyslexic people are better identified by writing that does not seem to match their level of intelligence from prior observations. Additionally, dyslexic people often substitute similar-looking, but unrelated, words in place of the ones intended (what/want, say/saw, help/held, run/fun, fell/fall, to/too, etc.).

## Comorbidities

Several learning disabilities often occur with dyslexia, but it is unclear whether these learning disabilities share underlying neurological causes with dyslexia. These disabilities include, but are not limited to:

- Dysgraphia— a disorder which expresses itself primarily through writing or typing, although in some cases it may also affect eye–hand coordination direction or sequence oriented processes such as tying knots or carrying out a repetitive task. In dyslexia, dysgraphia is often multifactorial, due to impaired letter writing automaticity, finger motor sequencing challenges, organizational and elaborative difficulties, and impaired visual word form which makes it more difficult to retrieve the visual picture of words required for spelling. Dysgraphia is distinct from dyspraxia in that dyspraxia is simply related motor sequence impairment.
- Dyscalculia— a neurological condition characterized by a problem with basic sense of number and quantity and difficult retrieving rote math facts. Often people with this condition can understand very complex mathematical concepts and principles but have difficulty retrieving basic math facts involving addition and subtraction.
- Attention Deficit Disorder — a high degree of co-morbidity has been reported between ADD / ADHD and dyslexia, although the contributions of dyslexia-related challenges such auditory verbal working memory to attention issues has not been well established
- Cluttering— a speech fluency disorder involving both the rate and rhythm of speech, resulting in impaired speech intelligibility. Speech is erratic and nonrhythmic, consisting of rapid and jerky spurts that usually involve faulty phrasing. The personality of people with cluttering bears striking resemblance to the personalities of those with learning disabilities.

## *Cause*

The following theories should not be viewed as competing, but viewed as theories trying to explain the underlying causes of a similar set of symptoms from a variety of research perspectives and background.

Cerebellar theory

The Cerebellar Theory asserts that a mildly dysfunctional cerebellum can cause dyslexia. The cerebellum contributes to motor control during the articulation of speech, and the Cerebellar Theory proposes that articulation problems can contribute to the phonological processing deficits that can cause dyslexia. The Cerebellum also contributes to the automatisation of learnt behaviors, which includes learning the grapheme–phoneme relationships when reading text.

Evolutionary hypothesis

This theory considers that reading is an unnatural act carried out by humans for an exceedingly brief period in our evolutionary history. It has been less than a hundred years that western societies promoted reading to the mass population and therefore the forces that shape our reading behavior have been weak. Many areas of the world still do not even have access to reading for the majority of the population.

Magnocellular theory

The Magnocellular theory attempts to unify the Cerebellar Theory, the Phonological Theory, the Rapid Auditory Processing Theory, and the Visual Theory. The Magnocellular theory proposes that the magnocellular dysfunction is not only restricted to the visual pathways but also includes auditory and tactile modalities.

Naming speed deficit and double deficit theories

The speed with which an individual can engage in the rapid automatized naming of familiar objects or letters is a strong predictor of dyslexia. Slow naming speed can be identified as early as kindergarten and persists in adults with dyslexia.

A deficit in naming speed is hypothesized to represent a deficit that is separate from phonological processing deficit. Wolf identified four types of readers: readers with no deficits, readers with phonological processing deficit, readers with naming speed deficit, and readers with double deficit (that is, problems both with phonological processing and naming speed). Students with double deficits are most likely to have some sort of severe reading impairment.

Distinguishing among these deficits has important implications for instructional intervention. If students with double deficits receive instruction only in phonological processing, they are only receiving part of what they need.

Perceptual visual-noise exclusion hypothesis

The concept of a perceptual noise exclusion deficit (impaired filtering of behaviorally irrelevant visual information in dyslexia or visual-noise) is an emerging hypothesis, supported by research showing that subjects with dyslexia experience difficulty in performing visual tasks (such as motion detection in the presence of perceptual distractions) but do not show the same impairment when the distracting factors are removed in an experimental setting. The researchers have analogized their findings concerning visual discrimination tasks to findings in other research related to auditory discrimination tasks. They assert that dyslexic symptoms arise because of an impaired ability to filter out both visual and auditory distractions, and to categorize information so as to distinguish the important sensory data from the irrelevant.

Phonological deficit theory

The phonological deficit theory proposes that people with dyslexia have a specific sound manipulation impairment, which affects their auditory memory, word recall, and sound association skills when processing speech. The phonological theory explains a reading impairment when using an alphabetic writing system which requires learning the grapheme/phoneme correspondence, the relationship between the graphic letter symbols and speech sounds which they represent.

Rapid auditory processing theory

The rapid auditory processing theory is an alternative to the phonological deficit theory, which specifies that the primary deficit lies in the perception of short or rapidly varying sounds. Support for this theory arises from evidence that people with dyslexia show poor performance on a number of auditory tasks, including frequency discrimination and temporal order judgment.

Visual theory

The visual theory represents a traditional perspective of dyslexia, as being the result of a visual impairment creating problems when processing information from letters and words from a written text. This includes visual processing problems such as binocular, poor vergence, and visual crowding. The Visual Theory does not deny the possibility of alternative causes of dyslexia

## Effect of language orthography

The complexity of a language's orthography or spelling system – formally, its orthographic depth – has a direct impact on how difficult it is to learn to read that language. English has a comparatively deep orthography within the Latin alphabet writing system, with a complex orthographic structure that employs spelling patterns at several levels: principally, letter-sound correspondences, syllables, and morphemes. Other languages, such as Spanish, have alphabetic orthographies that employ only letter-

sound correspondences, so-called shallow orthographies. It is relatively easy to learn to read languages like Spanish; it is much more difficult to learn to read languages with more complex orthographies, such as English. Logographic writing systems, notably Japanese and Chinese characters, have a purer direct relationship between the sound of a word and the representative visual symbols, which pose a different type of dyslexic difficulty.

From a neurological perspective, different types of writing system, for example alphabetic as compared to logographic writing systems, require different neurological pathways in order to read, write and spell. Because different writing systems require different parts of the brain to process the visual notation of speech, children with reading problems in one language might not have a reading problem in a language with a different orthography. The neurological skills required to perform the tasks of reading, writing, and spelling can vary between different writing systems and as a result different neurological deficits can cause dyslexic problems in relation to different orthographies.

## Exacerbating conditions

Dyslexia is attributed to neurological factors that influence the individual's ability to read, write, and spell written language.

The following conditions may be contributory or overlapping factors, as they can lead to difficulty in reading:

- Aphasia - neurologically based speech disorders, which can cause alexia (acquired dyslexia).
- Attention deficit hyperactivity disorder - A disorder that occurs in between 12% and 24% of those with dyslexia.
- Auditory processing disorder - A condition that affects the ability to process auditory information. Auditory processing disorder is a listening disability. It can lead to problems with auditory memory and auditory sequencing. Many people with dyslexia have auditory processing problems including history of auditory reversals, and may develop their own logographic cues to compensate for this type of deficit. Auditory processing disorder is recognized as one of the major causes of dyslexia. Some children can acquire auditory processing disorder as a result of experiencing otitis media with effusion (glue ear, sticky ear, grommets) and other severe ear conditions.
- Developmental dyspraxia - A neurological condition characterized by a marked difficulty in carrying out routine tasks involving balance, fine-motor control, kinesthetic coordination, difficulty in the use of speech sounds, problems with short term memory and organization are typical of dyspraxics.
- Scotopic sensitivity syndrome, also known as *Irlen Syndrome* - A term used to describe sensitivity to certain wavelengths of light which interfere with visual processing.
- Specific language impairment (SLI) - A developmental language disorder that can affect both expressive and receptive language. SLI is defined as a "pure" language

impairment, meaning that is not related to or caused by other developmental disorders, hearing loss or acquired brain injury. A study by the Universities of Maastricht and Utrecht examined speech perception and speech production in 3-year-old Dutch children at familial risk of developing dyslexia. Their performance in speech sound categorization and their production of words was compared to that of age-matched children with SLI and typically developing controls. The results of the at-risk and SLI-group were highly similar. Analysis of the individual data revealed that both groups contained subgroups with good and poorly performing children. Their impaired expressive phonology seemed to be related to a deficit in speech perception. The findings indicate that both dyslexia and SLI can be explained by a multi-risk model which includes cognitive processes as well as genetic factors.

Experience of speech acquisition delays and speech and language problems can be due to problems processing and decoding auditory input prior to reproducing their own version of speech, and may be observed as stuttering, cluttering or hesitant speech.

## *Management*

There is no cure for dyslexia, but dyslexic individuals can learn to read and write with appropriate educational support.

Especially for undergraduates, some consideration of what 'reading' is and what it is for can be useful. There are techniques (reading the first sentence [and/or last] of each paragraph in a chapter, for example) which can give an overview of content. This can be sufficient for some purposes. Since stress and anxiety are contributors to a dyslexic's weaknesses in absorbing information, removing these can assist in improving understanding. When a dyslexic knows that not every reading experience must be onerous, it greatly helps their mental approach to the task.

The best approaches acknowledge that the objective in helping to improve a dyslexic's 'reading' is not to 'read-like-a-non-dyslexic-does', but to find a way of extracting information from text that works efficiently for someone who processes such information differently from the majority.

For alphabet writing systems the fundamental aim is to increase a child's awareness of correspondences between graphemes and phonemes, and to relate these to reading and spelling. It has been found that training focused towards visual language and orthographic issues yields longer-lasting gains than mere oral phonological training.

The best form of approach is determined by the underlying neurological cause(s) of the dyslexic symptoms.

Context sensitive spell checkers combined with text-to-speech systems offer forms of assistive technology to dyslexia users, supporting reading and writing.

Recent research suggests that adaptive working memory training using a program called Jungle Memory was effective in boosting IQ, working memory, and literacy scores in students with dyslexia.

## *History*

- Identified by Oswald Berkhan in 1881, the term 'dyslexia' was later coined in 1887 by Rudolf Berlin, an ophthalmologist practising in Stuttgart, Germany, from the Greek prefix δυσ- (*dus*-), "hard, bad, difficult" + λέξις (*lexis*), "speech, word".
- In 1896, W. Pringle Morgan published a description of a reading-specific learning disorder in the British Medical Journal titled "Congenital Word Blindness".
- During the 1890s and early 1900s, James Hinshelwood published a series of articles in medical journals describing similar cases of congenital word blindness. In his 1917 book *Congenital Word Blindness*, Hinshelwood asserted that the primary disability was in visual memory for words and letters, and described symptoms including letter reversals, and difficulties with spelling and reading comprehension.
- **1925** Samuel T. Orton determined that there was a syndrome unrelated to brain damage that made learning to read difficult. Orton's theory strephosymbolia described individuals with dyslexia having difficulty associating the visual forms of words with their spoken forms. Orton observed that reading deficits in dyslexia did not seem to stem from strictly visual deficits. He believed the condition was caused by the failure to establish hemispheric dominance in the brain. Orton later worked with the psychologist and educator Anna Gillingham to develop an educational intervention that pioneered the use of simultaneous multisensory instruction.
- In contrast, Dearborn, Gates, Bennet and Blau considered a faulty guidance of the seeing mechanism to be the cause. They sought to discover if a conflict between spontaneous orientation of the scanning action of the eyes from right to left and training aimed at the acquisition of an opposite direction would allow an interpretation of the facts observed in the dyslexic disorder and especially of the ability to mirror-read.
- **1949** Research conducted under G. Mahec show that the phenomenon is clearly linked to the dynamics of sight as it disappears when the space between letters is increased, transforming the reading into spelling. This experience also explains the ability to mirror-read.
- **1968** Makita suggested that dyslexia was mostly absent among Japanese children. A 2005 study shows that Makita's claim of rarity of incidence of reading disabilities in Japan to be incorrect.
- In the 1970s a new hypothesis emerged: that dyslexia stems from a deficit in phonological processing or difficulty in recognizing that spoken words are formed by discrete phonemes. Affected individuals have difficulty associating these sounds with the visual letters that make up written words. Key studies suggested the importance of phonological awareness,
- **1979** Galaburda and Kemper, and Galaburda et al. 1985, reported observations from the examination of post autopsy brains of people with dyslexia. Their studies

reporting observed anatomical differences in the language center in a dyslexic brain, taken with the similar work of Cohen et al. 1989, suggested abnormal cortical development, which was presumed to occur before or during the sixth month of foetal brain development.

- **1993** Castles and Coltheart describe developmental dyslexia as two prevalent and distinct varieties using the subtypes of Alexia, Surface and Phonological Dyslexia. Manis et al. 1996, concluded that there were probably more than two subtypes of dyslexia, which would be related to multiple underlying deficits. Cestnick and Coltheart (1999) demonstrated what these underlying deficits are in part, through unveiling different profiles of phonological versus surface dyslexics. Cestnick and Jerger (2000) and Cestnick (2001) further demonstrated distinct processing differences between phonological and surface dyslexics.
- **1994** From post autopsy specimens Galaburda et al., reported: Abnormal auditory processing in people with dyslexia suggests that accompanying anatomical abnormalities might be present in the auditory system. Supported the reported behavioral findings of a left hemisphere-based phonological defect in dyslexic individuals.
- The development of neuroimaging technologies during the 1980s and 1990s enabled dyslexia research to make significant advances. Positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) studies have revealed the neural signature of adult normal reading (e.g. Fiez and Petersen, 1998; Turkeltaub et al., 2002 and phonological processing (e.g., Gelfand and Bookheimer, 2003; Poldrack et al., 1999). Employing various experimental approaches and paradigms (e.g., the detection or judgment of rhymes, nonword reading, and implicit reading), these studies have localized dysfunctional phonological processing in dyslexia to left-hemisphere perisylvian regions, especially for the alphabetic writing system. However, it has been demonstrated that in nonalphabetic scripts, where reading places less demands on phonemic processing and the integration of visual-orthographic information is crucial, dyslexia is associated with under activity of the left middle frontal gyrus (Siok et al., 2004).
- **1999** Wydell and Butterworth reported the case study of an English-Japanese bilingual with monolingual dyslexia. Suggesting that any language where orthography-to-phonology mapping is transparent, or even opaque, or any language whose orthographic unit representing sound is coarse (i.e. at a whole character or word level) should not produce a high incidence of developmental phonological dyslexia, and that orthography can influence dyslexic symptoms.
- **2003** Ziegler and colleagues claimed that the dyslexia suffered by German or Italian dyslexics is very similar to the one suffered by English dyslexics (readers of different—shallow versus deep orthographic systems), supporting the idea that the origin of dyslexia is mostly biological.
- **2007** Lyytinen et al. Researchers are seeking a link between the neurological and genetic findings, and the reading disorder.
- **2008** S Heim et al. in a paper titled "Cognitive subtypes of dyslexia" describe how they compared different sub-groups of dyslexics in comparison with a control group. This is one of the first studies not to just compare dyslexics with a non

dyslexic control, but to go further and compared the different cognitive sub groups with a non dyslexic control group.
- **2008** Wai Ting Siok et al. in a paper titled "A structural–functional basis for dyslexia in the cortex of Chinese readers" describe how dyslexia is language dependent, and especially between alphabetic and non-alphabetic writing systems.
- **2010** KK Chung et al. investigated the "Cognitive profiles of Hong Kong Chinese adolescents with dyslexia".

## *Society*

### Education law

There are many different national legal statutes and different national special education support structures with regard to special education provision which relate to the management of dyslexia.

## *Research*

The majority of currently available dyslexia research relates to the alphabetic writing system, and especially to languages of European origin. However, substantial research is also available regarding dyslexia for speakers of Arabic, Chinese, and Hebrew.

### Neuroimaging

Modern neuroimaging techniques such as functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) have produced clear evidence of structural differences in the brains of children with reading difficulties. It has been found that people with dyslexia have a deficit in parts of the left hemisphere of the brain involved in reading, which includes the inferior frontal gyrus, inferior parietal lobule, and middle and ventral temporal cortex.

That dyslexia is neurobiological in origin is supported by what Lyon et al. proclaimed as "overwhelming and converging data from functional brain imaging investigations" (2003, p. 3). The results of these studies suggest that there are observable differences in how the dyslexic brain functions when compared to the brain of a typical reader. Using fMRI, Shaywitz found that good readers show a consistent pattern of strong activation in the back of the brain with weaker activation in the front of the brain during reading tasks. In contrast, the brain activation pattern in dyslexics is the opposite during reading tasks—the frontal part of the brain becomes overactive with weaker activation in the back. Shaywitz points out *"It is as if these struggling readers are using the systems in the front of the brain to try to compensate for the disruption in the back of the brain."*

Brain activation studies using PET to study language have produced a breakthrough in understanding of the neural basis of language over the past decade. A neural basis for the visual lexicon and for auditory verbal short term memory components have been

proposed, with some implication that the observed neural manifestation of developmental dyslexia is task-specific (i.e., functional rather than structural).

A University of Hong Kong study argues that dyslexia affects different structural parts of children's brains depending on the language which the children read. The study focused on comparing children that were raised reading English and children raised reading Chinese. This is supported in a review by T. Hadzibeganovic et al. (2010).

A University of Maastricht (Netherlands) study revealed that adult dyslexic readers underactivate superior temporal cortex for the integration of letters and speech sounds.

## Genetic

Molecular studies have linked several forms of dyslexia to genetic markers for dyslexia. Several candidate genes have been identified, including at the two regions first related to dyslexia: DCDC2 and KIAA0319 on chromosome 6, and DYX1C1 on chromosome 15.

A 2007 review reported that no specific cognitive processes are known to be influenced by the proposed susceptibility genes.

A unifying theoretical framework of three working memory components provides a systems perspective for discussing past and new findings in a 12-year research program that point to heterogeneity in the genetic and brain basis and behavioral expression of dyslexia.

## Controversy

In recent years there has been significant debate on the categorization of dyslexia. In particular, Elliot and Gibbs argue that "attempts to distinguish between categories of 'dyslexia' and 'poor reader' or 'reading disabled' are scientifically unsupportable, arbitrary and thus potentially discriminatory".

While acknowledging that reading disability is a valid scientific curiosity, and that "seeking greater understanding of the relationship between visual symbols and spoken language is crucial" and that while there was "potential of genetics and neuroscience for guiding assessment and educational practice at some stage in the future", they conclude that "there is a mistaken belief that current knowledge in these fields is sufficient to justify a category of dyslexia as a subset of those who encounter reading difficulties".

# Chapter 2

# History of Developmental Dyslexia

Identified by Oswald Berkhan in 1881, the term 'dyslexia' was later coined in 1887 by Rudolf Berlin, an ophthalmologist practicing in Stuttgart, Germany. He used the term to refer to a case of a young boy who had a severe impairment in learning to read and write in spite of showing typical intellectual and physical abilities in all other respects.

In 1896, W. Pringle Morgan, a British physician, from Seaford, East Sussex published a description of a reading-specific learning disorder in a report to the British Medical Journal titled "Congenital Word Blindness". This described the case of a 14-year-old boy who had not yet learned to read, yet showed normal intelligence and was generally adept at other activities typical of children of that age.

## *1900-1950*

During the 1890s and early 1900s, James Hinshelwood, a British ophthalmologist, published a series of articles in medical journals describing similar cases of congenital word blindness, which he defined as "a congenital defect occurring in children with otherwise normal and undamaged brains characterised by a difficulty in learning to read." In his 1917 book *Congenital Word Blindness*, Hinshelwood asserted that the primary disability was in visual memory for words and letters, and described symptoms including letter reversals, and difficulties with spelling and reading comprehension.

In 1925 Samuel T. Orton, a neurologist who worked primarily with stroke victims, met a boy who could not read and who exhibited symptoms similar to stroke victims who had lost the ability to read. Orton began studying reading difficulties and determined that there was a syndrome unrelated to brain damage that made learning to read difficult. Orton called his theory strephosymbolia (meaning 'twisted signs') to describe individuals with dyslexia had difficulty associating the visual forms of words with their spoken forms. Orton observed that reading deficits in dyslexia did not seem to stem from strictly visual deficits. He believed the condition was caused by the failure to establish hemispheric dominance in the brain. He also observed that the children he worked with were disproportionately left- or mixed-handed, although this finding has been difficult to replicate. Influenced by the kinesthetic work of Helen Keller and Grace Fernald, and looking for a way to teach reading using both left and right brain functions, Orton later worked with psychologist and educator Anna Gillingham to develop an educational intervention that pioneered the use of simultaneous multisensory instruction.

In contrast, Dearborn, Gates, Bennet and Blau considered a faulty guidance of the seeing mechanism to be the cause. They sought to discover if a conflict between spontaneous orientation of the scanning action of the eyes from right to left and training aimed at the acquisition of an opposite direction would allow an interpretation of the facts observed in the dyslexic disorder and especially of the ability to mirror-read. To this end the authors asked four adults to read a text reflected in a mirror for ten minutes a day for five months. In all subjects, the words were not perceived in their globality but required a meticulous analysis of the letters and syllables. They also demonstrated total or partial inversions even sometimes affecting the order of the words in a sentence. They revealed a curious impression of not just horizontal but also vertical inversions. These are errors that exist amongst people with dyslexia and they suffer from the aggravating circumstance inherent in all learning.

## *1950-2000*

1949 research conducted under Clement Launay (thesis G. Mahec Paris 1951) went further. In adult subjects, the reading of a series of 66 tiny lower-case letters, 5 mm high, spaced 5 mm apart, first from left to right, and then from right to left, was more easily and quickly done in the left to right direction. For former dyslexic children, a substantial number read a series of 42 letters with equal speed in both directions, and some (10%) read better from right to left than from left to right. The phenomenon is clearly linked to the dynamics of sight, as it disappears when the space between letters is increased, transforming the reading into spelling. This experience also explains the ability to mirror-read.

In the 1970s, a new hypothesis emerged that dyslexia stems from a deficit in phonological processing, or difficulty in recognizing that spoken words are formed by discrete phonemes, (for example, that the word CAT comes from the sounds [k], [æ], and [t]). As a result, affected individuals have difficulty associating these sounds with the visual letters that make up written words. Key studies of the phonological deficit hypothesis include the finding that the strongest predictor of reading success in school age children is phonological awareness and that phonological awareness instruction can improve decoding skills for children with reading difficulties.

In 1979 Galaburda and Kemper, and Galaburda et al. 1985, from the examination of post autopsy brains of people with dyslexia. Observed anatomical differences in the language center in a dyslexic brain, showing microscopic cortical malformations known as ectopias and more rarely vascular micro-malformations and in some instances these cortical malformations appeared as a microgyrus. These studies and those of Cohen et al. 1989, suggested abnormal cortical development which was presumed to occur before or during the sixth month of foetal brain development.

1993 Castles and Coltheart describe developmental dyslexia as two prevalent and distinct varieties using the subtypes of Alexia, Surface and Phonological Dyslexia. Understanding these subtypes is useful in diagnosing learning patterns and developing approaches for overcoming visual perception impairments or speech discrimination deficits. Surface

Dyslexia is characterized by subjects who can read known words but who have trouble reading words that are irregular. Phonological Dyslexia is characterized by subjects who can read aloud both regular and irregular words but have difficulties with non-words and with connecting sounds to symbols, or with sounding out words. Phonological processing tasks predict reading accuracy and comprehension. Manis et al. 1996, concluded that there were probably more than two subtypes of dyslexia, which would be related to multiple underlying deficits.

1994 From post autopsy specimens Galaburda et al., reported : Abnormal auditory processing in people with dyslexia suggests that accompanying anatomical abnormalities might be present in the auditory system. They measured cross-sectional neuronal areas in the medial geniculate nuclei (MGNs) of five dyslexic and seven control brains. In contrast to controls, which showed no asymmetry, the left-side medial geniculate nucleus (MGN) neurons were significantly smaller than the right in the dyslexic sample. Also, as compared with controls, there were more small neurons and fewer large neurons in the left dyslexic MGN. These findings are consistent with reported behavioral findings of a left hemisphere-based phonological defect in dyslexic individuals.

The development of **Neuroimaging** technologies during the 1980s and 1990s enabled dyslexia research to make significant advances. Positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) studies have revealed the neural signature of adult normal reading (e.g.,Bookheimer et al., 1995; Fiez and Petersen, 1998; Price, 1997; Pugh et al., 1996; Turkeltaub et al., 2002) and phonological processing (e.g., Gelfand and Bookheimer, 2003; Poldrack et al., 1999; Price et al., 1997; Rumsey et al., 1997a). Brain imaging studies have also characterized the anomalous patterns of neuronal activation associated with reading and phonological processing in adults with persistent or compensated developmental dyslexia (e.g., Brunswick et al., 1999; Demonet et al., 1992; Flowers et al., 1991; Horwitz et al., 1998; Ingvar et al., 1993; Paulesu et al., 1996; Pugh et al., 2000; Rumsey et al., 1997b; Shaywitz et al., 1998 ). Employing various experimental approaches and paradigms (e.g., the detection or judgment of rhymes, nonword reading, and implicit reading), these studies have localized dysfunctional phonological processing in dyslexia to left-hemisphere perisylvian regions. Differences in task-related signal change in the left temporoparietal and occipitotemporal cortices have emerged as the most consistent findings in studies of dyslexia in the alphabetic writing system. However, it has been demonstrated that in nonalphabetic scripts, where reading places less demands on phonemic processing and the integration of visual-orthographic information is crucial, dyslexia is associated with under activity of the left middle frontal gyrus (Siok et al., 2004).

## *2000s*

1999 Wydell and Butterworth reported the case study of an English-Japanese bilingual with monolingual dyslexia. Suggesting that any language where orthography-to-phonology mapping is transparent, or even opaque, or any language whose orthographic unit representing sound is coarse (i.e. at a whole character or word level) should not

produce a high incidence of developmental phonological dyslexia, and that orthograpy can influence dyslexic symptoms

2001 Temple et al. Suggest that dyslexia may be characterized in childhood by disruptions in the neural bases of both phonological and orthographic processes important for reading.

2002 Talcott et al. reported that both visual motion sensitivity and auditory sensitivity to frequency differences were robust predictors of children's literacy skills and their orthographic and phonological skills.

2003 Turkeltaub et al., reported: "The complexities of pediatric brain imaging have precluded studies that trace the neural development of cognitive skills acquired during childhood. Using a task that isolates reading-related brain activity and minimizes confounding performance effects, we carried out a cross-sectional functional magnetic resonance imaging (fMRI) study using subjects whose ages ranged from 6 to 22 years. We found that learning to read is associated with two patterns of change in brain activity: increased activity in left-hemisphere middle temporal and Inferior frontal gyrus and decreased activity in right inferotemporal cortica areas. Activity in the left-posterior superior temporal sulcus of the youngest readers was associated with the maturation of their phonological processing abilities. These findings inform current reading models and provide strong support for Orton's 1925 theory of reading development."

(A guide to the areas of the brain List of regions in the human brain, Cerebral hemisphere. and Cerebral cortex )

2003 Current models of the relation between the brain and dyslexia generally focus on some form of defective or delayed brain maturation. More recently, genetic research has provided increasing evidence supporting a genetic origin of dyslexia.

2004 A University of Hong Kong study argues that dyslexia affects different structural parts of children's brains depending on the language which the children read.

2007 Researchers are searching for a link between the neurological and genetic findings, and the reading disorder. There are many previous and current theories of dyslexia, but one that has much support from research is that, whatever the biological cause, dyslexia is a matter of reduced phonogical awareness, the ability to analyze and link the units of spoken and written languages.

2008 S Heim et al. This is one of the first studies not to just compare dyslexics with a non dyslexic control, but to go further and compared the different cognitive sub groups with a non dyslexic control group. Different theories conceptualise dyslexia as either a phonological, attentional, auditory, magnocellular, or automatisation deficit. Such heterogeneity suggests the existence of yet unrecognised subtypes of dyslexics suffering from distinguishable deficits. The purpose of the study was to identify cognitive subtypes of dyslexia. Out of 642 children screened for reading ability 49 dyslexics and 48 controls

were tested for phonological awareness, auditory discrimination, motion detection, visual attention, and rhythm imitation. A combined cluster and discriminant analysis approach revealed three clusters of dyslexics with different cognitive deficits. Compared to reading-unimpaired children cluster no. 1 had worse phonological awareness; cluster no. 2 had higher attentional costs; cluster no. 3 performed worse in the phonological, auditory, and magnocellular tasks. These results indicate that dyslexia may result from distinct cognitive impairments. As a consequence, prevention and remediation programmes should be specifically targeted for the individual child's deficit pattern.

# Chapter 3

# Characteristics of Dyslexia

The characteristics of **dyslexia** have been identified mainly from research in languages with alphabetic writing systems, primarily English. However, many of these characteristic may be transferable to other types of writing systems.

## *Listening, speech and language*

Some shared symptoms of the speech/hearing deficits and dyslexia:

1. Confusion with before/after, right/left, and so on
2. Difficulty learning the alphabet
3. Difficulty with word retrieval or naming problems
4. Difficulty identifying or generating rhyming words, or counting syllables in words (phonological awareness)
5. Difficulty with hearing and manipulating sounds in words (phonemic awareness)
6. Difficulty distinguishing different sounds in words (auditory discrimination)
7. Difficulty in learning the sounds of letters
8. Difficulty associating individual words with their correct meanings
9. Difficulty with time keeping and concept of time
10. Confusion with combinations of words
11. Difficulty in organization skills

The identification of these factors results from the study of patterns across many clinical observations of dyslexic children. In the UK, Thomas Richard Miles was important in such work and his observations led him to develop the Bangor Dyslexia Diagnostic Test.

Dyslexia is about having problems with the visual notation of speech, which in most languages of European origin are problems with alphabet writing systems which have a phonetic construction. Experience of speech acquisition delays, and speech and language problems can be due to problems processing and decoding auditory input prior to reproducing their own version of speech, and may be observed as stuttering, cluttering or hesitant speech. There are a range of neurological issues in Speech and Language Pathology which can later cause problems accessing the visual notation of speech, dyslexic problems. Examples of these issues can be problems speaking in full sentences, problems correctly articulating Rs and Ls as well as Ms and Ns, mixing up sounds in multi-syllabic words (ex: aminal for animal, bisghetti for spaghetti, hekalopter for

helicopter, hangaberg for hamburger, ageen for magazine, etc.), problems of immature speech "wed and gween" instead of "red and green". Some of these speech related problems can be caused by auditory processing disorder issues. Which can create a neurological auditory barrier to developing good phonological awareness skills, as a result some may develop alternative skills and which are based on recognising alphabetic words by their visual shape or Whole language and developing Logographic cues.

## *Reading and spelling*

- Spelling errors — Because of difficulty learning letter-sound correspondences, individuals with dyslexia might tend to misspell words, or leave vowels out of words.
- Letter order - People with dyslexia may also reverse the order of two letters especially when the final, incorrect, word looks similar to the intended word (e.g., spelling "dose" instead of "does").
- Letter addition/subtraction - People with dyslexia may perceive a word with letters added, subtracted, or repeated. This can lead to confusion between two words containing most of the same letters.
- Highly phoneticized spelling - People with dyslexia also commonly spell words inconsistently, but in a highly phonetic form such as writing "shud" for "should". Dyslexic individuals also typically have difficulty distinguishing among homophones such as "their" and "there".
- Vocabulary - Having a small written vocabulary, even if they have a large spoken vocabulary.

## *Writing and motor skills*

Because of literacy problems, an individual with dyslexia may have difficulty with handwriting. This can involve slower writing speed than average, poor handwriting characterised by irregularly formed letters, or inability to write straight on a blank paper with no guideline.

Some studies have also reported gross motor difficulties in dyslexia, including motor skills disorder. This difficulty is indicated by clumsiness and poor coordination. The relationship between motor skills and reading difficulties is poorly understood but could be linked to the role of the cerebellum and inner ear in the development of reading and motor abilities.

## *Mathematical abilities*

Dyslexia and dyscalculia are two learning disorders with different cognitive profiles. Dyslexia and dyscalculia have separable cognitive profiles, namely a phonological deficit in the case of dyslexia and a deficient number module in the case of dyscalculia.

Individuals with dyslexia can be gifted in mathematics while having poor reading skills. They might have difficulty with word processing problems. (i.e., descriptive

mathematics, engineering, or physics problems that rely on written text rather than numbers or formulas).

## *Adaptive attributes*

A study has found that entrepreneurs are five times more likely to be dyslexic than average citizens.

Evidence based on randomly selected populations of children indicate that dyslexia affects boys and girls equally; that dyslexia is diagnosed more frequently in boys appears to be the result of sampling bias in school-identified sample populations.

In the United States, researchers estimate the prevalence of dyslexia to range from three to ten percent of school-aged children though some have put the figure as high as 17 percent. Recent studies indicate that dyslexia is particularly prevalent among small business owners, with roughly 20 to 35 percent of U. S. and British entrepreneurs being affected.

# Chapter 4

# Dysgraphia

| Agraphia | |
|---|---|
| **ICD-10** | F81.1, R48.8 |
| **ICD-9** | 315.2, 784.61, 784.69 |
| **MeSH** | D000381 |

**Dysgraphia** (or **agraphia**) is a deficiency in the ability to write, regardless of the ability to read, not due to intellectual impairment.

People with dysgraphia usually can write on some level, and often lack other fine motor skills and may be cross dominant, finding tasks such as tying shoes difficult. It often does not affect all fine motor skills. They can also lack basic grammar and spelling skills (for example, having difficulties with the letters p, q, b, and d), and often will write the wrong word when trying to formulate thoughts (on paper). In childhood, the disorder generally emerges when the child is first introduced to writing. The child may make inappropriately sized and spaced letters, or write wrong or misspelled words despite thorough instruction. Children with the disorder may have other learning disabilities, but they usually have no social or other academic problems. Cases of dysgraphia in adults generally occur after some neurological trauma. Dysgraphia may also be diagnosed in a person with Tourette syndrome, ADHD or an autism spectrum disorder such as Asperger syndrome. The DSM IV identifies dysgraphia as a "Disorder of Written Expression" as "writing skills (that) ...are substantially below those expected given the person's ...age, measured intelligence, and age-appropriate education."

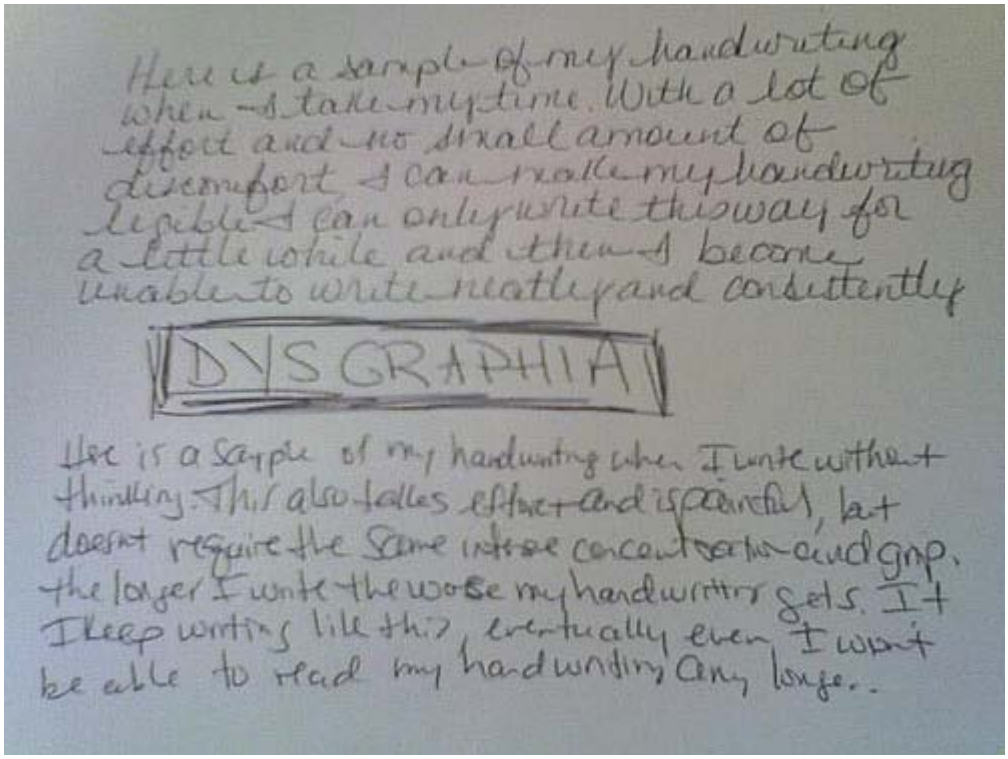
## *Types of dysgraphia*

Three principal subtypes of dysgraphia are recognized. Some children may have a combination of two or all three of these, and individual symptoms may vary in presentation from what is described here.

## Dyslexic dysgraphia

With dyslexic dysgraphia, spontaneously written work is illegible, copied work is fairly good, and spelling is bad. Finger tapping speed (a method for identifying fine motor problems) is normal, indicating the deficit does not likely stem from cerebellar damage. A dyslexic dysgraphic does not necessarily have dyslexia. (Dyslexia and dysgraphia appear to be unrelated but are often found together.)

## Motor dysgraphia




Example of motor dysgraphia in a 30-year-old female

Motor dysgraphia is due to deficient fine motor skills, poor dexterity, poor muscle tone, or unspecified motor clumsiness. Motor dysgraphia may be part of the larger problem of motor apraxia. Generally, written work is poor to illegible, even if copied by sight from another document. Letter formation may be acceptable in very short samples of writing, but this requires extreme effort and an unreasonable amount of time to accomplish, and cannot be sustained for a significant length of time. Writing long passages is extremely painful and cannot be sustained. Letter shape and size becomes increasingly inconsistent and illegible. Writing is often slanted due to holding a pen or pencil incorrectly. Spelling skills are not impaired. Finger tapping speed results are below normal.

### Spatial dysgraphia

A person with dysgraphia due to a defect in the understanding of space has illegible spontaneously written work, illegible copied work, but normal spelling and normal tapping speed.

## *Symptoms of dysgraphia*

A mixture of upper/lower case letters, irregular letter sizes and shapes, unfinished letters, struggle to use writing as a communications tool, odd writing grip, many spelling mistakes (sometimes), pain when writing, decreased or increased speed of writing and copying, talks to self while writing, muscle spasms in the arm and shoulder (sometimes in the rest of the body), inability to flex (sometimes move) the arm (creating an L-like shape), and general illegibility.

Many people who are dysgraphic experience pain while writing. The pain usually starts in the center of the forearm and then spreads along the nervous system to the entire body. This pain can get worse or even appear when a dysgraphic is stressed. Few people who do not have dysgraphia know about this, because many with dysgraphia will not mention it to anyone. There are a few reasons why pain while writing is rarely mentioned:

- Sufferers do not know that it is unusual to experience this type of pain with writing.
- If they know that it is different from how others experience writing, they feel that few will believe them.
- Those who do not believe that the pain while writing is real will often not understand it. It will usually be attributed to muscle ache or cramping, and it will often be considered only a minor inconvenience.
- For some people with dysgraphia, they no longer write, and just type everything, so they no longer feel this pain.

Dysgraphics who experience this pain may exhibit reluctance or refusal to complete writing tasks.

## *Common problems that are often associated with dysgraphia*

### Stress

There are some common problems not related to dysgraphia but often associated with dysgraphia, the most common of which is stress. Often children (and adults) with dysgraphia will become extremely frustrated with the task of writing (and spelling); younger children may cry or refuse to complete written assignments. This frustration can cause the child (or adult) a great deal of stress and can lead to stress-related illnesses. This can be a result of any symptom of dysgraphia.

## *Treatment*

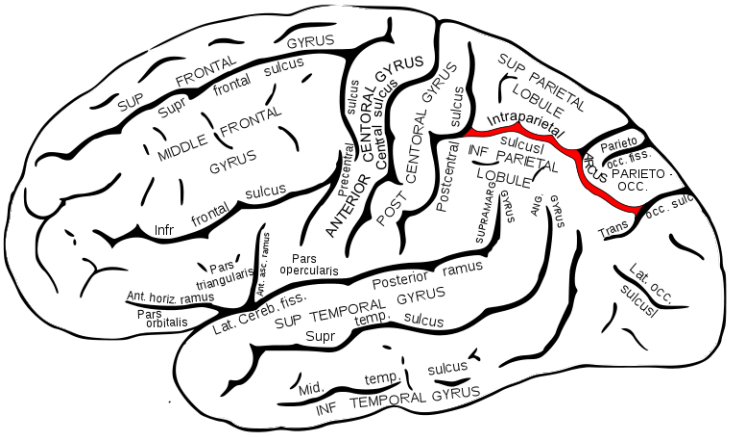
Treatment for dysgraphia varies and may include treatment for motor disorders to help control writing movements. Other treatments may address impaired memory or other neurological problems. Some physicians recommend that individuals with dysgraphia use computers to avoid the problems of handwriting.

Occupational therapy could be considered to strengthen muscle tone, improve dexterity, and evaluate eye–hand coordination. Dysgraphic children should also be evaluated for ambidexterity, which can delay fine motor skills in early childhood. Diagnosing dysgraphia can be challenging but can be done at facilities specializing in learning disabilities.

# Chapter 5

# Dyscalculia

**Dyscalculia**




Lateral surface of left cerebral hemisphere, viewed from the side.

(Intraparietal sulcus visible at upper right, running horizontally.)

| | |
|---|---|
| **ICD-10** | F81.2, R48.8 |
| **ICD-9** | 315.1, 784.69 |

**Dyscalculia** or **math disability** is a specific learning disability or difficulty involving innate difficulty in learning or comprehending mathematics. It is akin to dyslexia and can include confusion about math symbols. Dyscalculia can also occur as the result of some types of brain injury.

Dyscalculia occurs in people across the whole IQ range. Current estimates suggest it may affect about 5% of the population.

## *History*

The term dates back to at least 1974.

Dyscalculia was originally identified in case studies with patients who suffered specific arithmetic disabilities as a result of damage to specific regions of the brain. Recent

research suggests that dyscalculia can also occur developmentally, as a genetically-linked learning disability which affects a person's ability to understand, remember, or manipulate numbers or number facts (e.g., the multiplication tables). The term is often used to refer specifically to the inability to perform arithmetic operations, but it is also defined by some educational professionals and cognitive psychologists as a more fundamental inability to conceptualize numbers as abstract concepts of comparative quantities (a deficit in "number sense").

## *Etymology*

The word dyscalculia comes from Greek and Latin which means: "counting badly". The prefix "dys" comes from Greek and means "badly". "Calculia" comes from the Latin "calculare," which means "to count". The word "calculare" comes from "calculus", which means "pebble" or one of the counters on an abacus.

## *Synonym*

Numlexia - Synonym for Dyscalculia

## *Diagnosis*

Dyscalculia can be detected at a young age and measures can be taken to ease the problems faced by younger students. The main problem is understanding the way mathematics is taught to children. In the way that dyslexia can be dealt with by using a slightly different approach to teaching, so can dyscalculia. However, dyscalculia is the lesser known of these learning disorders and so is often not recognized.

## *Symptoms*

- Frequent difficulties with arithmetic, confusing the signs: +, −, ÷ and ×.
- Difficulty with everyday tasks like checking change and reading analog clocks.
- Inability to comprehend financial planning or budgeting, sometimes even at a basic level; for example, estimating the cost of the items in a shopping basket or balancing a checkbook.
- Difficulty with multiplication-tables, and subtraction-tables, addition tables, division tables, mental arithmetic, etc.
- May do fairly well in subjects such as science and geometry, which require logic rather than formulae, until a higher level requiring calculations is obtained.
- Many of those who suffer from dyscalculia may have parents who perform well to excellent in Mathematics-related fields (such as architects, engineers, or math teachers), though this connection has yet to be genetically linked.
- Difficulty with conceptualizing time and judging the passing of time. May be chronically late or early.
- Particularly problems with differentiating between left and right.
- Might do exceptionally well in a writing related field- many authors and journalists have this disorder

- Difficulty navigating or mentally "turning" the map to face the current direction rather than the common North=Top usage.
- Having particular difficulty mentally estimating the measurement of an object or distance (e.g., whether something is 10 or 20 feet (3 or 6 metres) away).
- Often unable to grasp and remember mathematical concepts, rules, formulae, and sequences.
- An inability to read a sequence of numbers, or transposing them when repeated, such as turning 56 into 65.
- Difficulty keeping score during games.
- Difficulty with games such as poker with more flexible rules for scoring.
- Difficulty in activities requiring sequential processing, from the physical (such as dance steps or sports) to the abstract (signaling things in the right order). May have trouble even with a calculator due to difficulties in the process of feeding in variables.
- The condition may lead in extreme cases to a phobia or durable anxiety of mathematics and mathematic-numeric devices/coherences.
- Inability to concentrate on mentally intensive tasks.
- Low latent inhibition, i.e., over-sensitivity to noise, smell, light and the inability to tune out, filtering unwanted information or impressions. Might have a well-developed sense of imagination due to this (possibly as cognitive compensation to mathematical-numeric deficits).
- Mistaken recollection of names. Poor name/face retrieval. May substitute names beginning with same letter.

## *Causes*

Scientists have yet to understand the causes of dyscalculia. They have been investigating in several domains.

- Neurological: Dyscalculia has been associated with lesions to the supramarginal and angular gyri at the junction between the temporal and parietal lobes of the cerebral cortex.

- Deficits in working memory: Adams and Hitch argue that working memory is a major factor in mental addition. From this base, Geary conducted a study that suggested there was a working memory deficit for those who suffered from dyscalculia. However, working memory problems are confounded with general learning difficulties, thus Geary's findings may not be specific to dyscalculia but rather may reflect a greater learning deficit.

Other causes may be:

- Short term memory being disturbed or reduced, making it difficult to remember calculations.
- Congenital or hereditary disorders. Studies show indications of this, but the evidence is not yet concrete.

Gerstmann syndrome: dyscalculia is one of a constellation of symptoms acquired after damage to the angular gyrus.

Involvement of the intraparietal sulcus has been suggested.

## *Treatment*

Some people with Dyscalculia have advocated a shift in attitudes toward the view that it is a difference, rather than a disability that must be treated or cured if they show talent in other areas - such as art skills.

Software intended to remediate dyscalculia has been developed.

A study published in Current Biology to "investigate the feasibility of using noninvasive stimulation to the parietal lobe during numerical learning to selectively improve numerical abilities" used transcranial direct current stimulation (TDCS) and demonstrated improvement that was still present six months later.

# Chapter 6

# Cluttering

| Cluttering | |
|---|---|
| **ICD-10** | F98.6 |
| **ICD-9** | 307.0 |

**Cluttering** (also called *tachyphemia*) is a speech disorder and a communication disorder characterized by speech that is difficult for listeners to understand due to rapid speaking rate, erratic rhythm, poor syntax or grammar, and words or groups of words unrelated to the sentence. Cluttering has in the past been viewed as a fluency disorder.

## *Definitions*

Cluttering has been in the process of being defined for the last forty years. A current definition of cluttering is:

Cluttering is a fluency disorder characterized by a rate that is perceived to be abnormally rapid, irregular, or both for the speaker (although measured syllable rates may not exceed normal limits). These rate abnormalities further are manifest in one or more of the following symptoms: (a) an excessive number of disfluencies, the majority of which are not typical of people with stuttering; (b) the frequent placement of pauses and use of prosodic patterns that do not conform to syntactic and semantic constraints; and (c) inappropriate (usually excessive) degrees of coarticulation among sounds, especially in multisyllabic words.

## *Presentation*

Those with cluttering may experience a short attention span, poor concentration, poorly organized thinking, inability to listen, and a lack of awareness that one's speech is unintelligible.

Spoonerisms, malapropisms, Colemanballs, and Freudian slips are examples of cluttering. Stuttering as a common term often refers to the speech disorder of cluttering, rather than to the speech disorder of stuttering. Cluttered speech is exhibited by normal

speakers, and is often referred to as stuttering—this is especially true when the speaker is nervous, where nervous speech more closely resembles cluttering than stuttering.

Cluttering is sometimes confused with *stuttering*. Both communication disorders break the normal flow of speech. However, while stuttering is most often analyzed as a speech disorder, cluttering is a language disorder. In other words, a stutterer has a coherent pattern of thoughts, but can't say it; in contrast, a clutterer has no problem putting thoughts into words, but those thoughts become disorganized during speaking. Cluttering not only affects speech, but affects thought patterns, writing, typing, and conversation.

Stutterers are usually dysfluent on initial sounds, when beginning to speak, and become more fluent towards the ends of utterances. In contrast, clutterers are most clear at the start of utterances, but their speaking rate increases and intelligibility decreases towards the end of utterances.

Stuttering is characterized by struggle behavior, such as overtense speech production muscles. Cluttering, in contrast, is effortless.

Cluttering is also characterized by slurred speech, especially dropped or distorted /r/ and /l/ sounds; and monotone speech that starts loud and trails off into a murmur.

Clutterers often also have reading and writing disorders, especially sprawling, disorderly handwriting, which poorly integrate ideas and space. A clutterer described the feeling associated with a clutter as:

> “ It feels like 1) about twenty thoughts explode on my mind all at once, and I need to express them all, 2) that when I'm trying to make a point, that I just remembered something that I was supposed to say, so the person can understand, and I need to interrupt myself to say something that I should have said before, and 3) that I need to constantly revise the sentences that I'm working on, to get it out right. ”

Another clutterer wrote on an Internet support group:

> “ I just seem to rush through the words, and often slur words together and/or mumble—and as a result I often have to slow down, concentrate, and repeat myself. ”

> “ I add words into my sentences; as an example, 'like', mostly when I'm explaining something or trying to tell someone what I did yesterday. It's getting really annoying and I can't help it. When I try not to say 'like', I just stop and I can't physically speak. ”

### Cluttering versus stuttering

Cluttering and stuttering sound very similar to the lay ear, especially when they are at their worst. However, they are markedly different disorders and clutterers and stutterers are very different.

Stutterers:

- Are very aware of their disorder
- Perform worse when speaking under stress
- Have a hard time fluently giving short answers
- Often have inhibited, neat handwriting
- Therapy focuses on relaxation techniques, calling attention away from speech
- Typically were fluent, but then started stuttering
- Know exactly what they want to say but cannot say it
- Have organized speech
- Have good listening skills

Clutterers:

- Are very unaware of their disorder
- Perform better when speaking under stress
- Have a hard time fluently giving long answers
- Have hasty, repetitious, uninhibited, messy handwriting
- Have little to no fear of their speech and are careless in speech
- Therapy focuses on calling attention to speech details
- Are typically outgoing or extroverted
- Typically were never very fluent
- Do know exactly what they want to say, but it becomes disorganized while actually speaking
- Have disorganized, tangential, grammatically incorrect speech with word substitutions
- Are impatient listeners, frequently interrupt, and have poor turn-taking skills in conversation

## *Related disorders*

Cluttering can often be confused with language delay, language disorder, learning disabilities, and attention deficit disorder. People with ADD or ADHD may have many of the same symptoms as clutterers, including being inattentive, restless, short tempered, and impatient.

## *Treatment*

Because clutterers have poor awareness of their disorder, they may be indifferent or even hostile to speech-language pathologists. Treatment for cluttering usually takes longer

than stuttering treatment. Delayed auditory feedback (DAF) is usually used to produce a more deliberate, exaggerated oral-motor response pattern. Other treatment components include improving narrative structure with story-telling picture books, turn-taking practice, pausing practice, and language therapy.

## History

Battaros was a legendary Libyan king who spoke quickly and in a disorderly fashion. Others who spoke as he did were said to suffer from *battarismus*. This is the earliest record of the speech disorder of cluttering.

In the 1960s, cluttering was called *tachyphemia*, a word derived from the Greek for "fast speech." This word is currently not used to describe cluttering because fast speech is not a required element of cluttering.

Deso Weiss described cluttering as the outward manifestation of a "central language imbalance." In Weiss's book on cluttering, he used Central Language Imbalance or CLI as synonymous with what cluttering is described as today.

Over the past twenty years, Kenneth O. St. Louis, Lawrence J. Raphael, Florence L. Myers, and Klaas Bakker have been working to standardize a definition of cluttering. Judith Kuster maintains a robust section of cluttering resources and articles in her Stuttering Homepage.

The first conference held specifically on cluttering was held in May 2007 in Razlog, Bulgaria. It was called, "The First World Conference on Cluttering," and had over 60 participants from across North America, Europe, the Middle East and Asia. It was held in Bulgaria partly because of cluttering research efforts by Professors Dobrinka Georgieva and Katya Dionissieva of Neofit Rilski. Part of the conference was awarding the first Deso Weiss Award for Excellence in Cluttering, which went to Kenneth St. Louis for his contributions for understanding and knowledge about cluttering.

## Cluttering researchers

Cluttering research is still in its infancy. Cluttering research peaked and faded away in the 1960s, but interest in cluttering research has drastically increased and there are numerous books on cluttering that are currently being written. Because of this renewed interest in cluttering, the current cluttering researchers are pioneers in this speech disorder. Most of the cluttering researchers were stuttering researchers who studied cluttering as a secondary behavior, however there are a few dedicated cluttering researchers. The most notable of the cluttering researchers are:

- Deso Weiss
- David Daly
- Charles Van Riper
- Florence Myers

- Kenneth St. Louis
- Klaas Bakker
- Judith Kuster
- Katerina de Hirsch
- Alf Preus
- Lawrence Raphael
- Yvonne van Zaalen

## *Famous clutterers*

Weiss claimed that Battaros, Demosthenes, Pericles, Justinian, Otto von Bismarck, and Winston Churchill were clutterers. He says about these people, "Each of these contributors to world history viewed his world holistically, and was not deflected by exaggerated attention to small details. Perhaps then, they excelled because of, rather than in spite of, their [cluttering]." The animated character Porky Pig, who has often been described as a stutterer, has a style of speech similar to cluttering in some ways.

# Chapter 7

# Theories of Dyslexia and Perceptual Noise Exclusion Hypothesis

## Theories of dyslexia

The primary symptoms of dyslexia were first identified by Oswald Berkhan in 1881. The term 'dyslexia' was coined in 1887 by Rudolf Berlin, an ophthalmologist practicing in Stuttgart, Germany. Since then generations of researchers have been investigating what dyslexia is and trying to identify the biological causes. The theories of the etiology of dyslexia have and are evolving with each new generation of dyslexia researchers, and the more recent theories of dyslexia tend to enhance one or more of the older theories as understanding of the nature of dyslexia evolves.

### *Theories of Developmental Dyslexia*

The following theories should not be viewed as competing, but viewed as theories trying to explain the underlying causes of a similar set of symptoms from a variety of research perspectives and background.

Cerebellar theory

The Cerebellar Theory asserts that a mildly dysfunctional cerebellum can cause dyslexia. The cerebellum contributes to motor control during the articulation of speech, and the Cerebellar Theory proposes that articulation problems can contribute to the phonological processing deficits that can cause dyslexia. The Cerebellum also contributes to the automatisation of learnt behaviors, which includes learning the grapheme–phoneme relationships when reading text.

Evolutionary hypothesis

This theory considers that reading is an unnatural act carried out for an very brief period in human evolutionary history. It has only been in the last hundred years that reading a visual form of speech has been promoted as a major form of communication, and subsequently a lack of time for reading behaviors to evolve. In many societies around the

world the majority of the population do not use the visual notation of speech as a form of communication, and do not use reading skills, and therefore have no dyslexia.

Magnocellular theory

The Magnocellular theory attempts to unify the Cerebellar Theory, the Phonological Theory, the Rapid Auditory Processing Theory, and the Visual Theory. The Magnocellular theory proposes that the magnocellular dysfunction is not only restricted to the visual pathways but also includes auditory and tactile modalities.

Naming speed deficit and double deficit theories

The speed with which an individual can engage in the rapid automatized naming of familiar objects or letters is a strong predictor of dyslexia. Slow naming speed can be identified as early as kindergarten and persists in adults with dyslexia.

A deficit in naming speed is hypothesized to represent a deficit that is separate from phonological processing deficit. Wolf identified four types of readers: readers with no deficits, readers with phonological processing deficit, readers with naming speed deficit, and readers with double deficit (that is, problems both with phonological processing and naming speed). Students with double deficits are most likely to have some sort of severe reading impairment.

Distinguishing among these deficits has important implications for instructional intervention. If students with double deficits receive instruction only in phonological processing, they are only receiving part of what they need.

Perceptual visual-noise exclusion hypothesis

The concept of a perceptual noise exclusion deficit (impaired filtering of behaviorally irrelevant visual information in dyslexia or visual-noise) is an emerging hypothesis, supported by research showing that subjects with dyslexia experience difficulty in performing visual tasks (such as motion detection in the presence of perceptual distractions) but do not show the same impairment when the distracting factors are removed in an experimental setting. The researchers have analogized their findings concerning visual discrimination tasks to findings in other research related to auditory discrimination tasks. They assert that dyslexic symptoms arise because of an impaired ability to filter out both visual and auditory distractions, and to categorize information so as to distinguish the important sensory data from the irrelevant.

Phonological deficit theory

The phonological deficit theory proposes that people with dyslexia have a specific sound manipulation impairment, which affects their auditory memory, word recall, and sound association skills when processing speech. The phonological theory explains a reading impairment when using an alphabetic writing system which requires learning the

grapheme/phoneme correspondence, the relationship between the graphic letter symbols and speech sounds which they represent.

Rapid auditory processing theory

The rapid auditory processing theory is an alternative to the phonological deficit theory, which specifies that the primary deficit lies in the perception of short or rapidly varying sounds. Support for this theory arises from evidence that people with dyslexia show poor performance on a number of auditory tasks, including frequency discrimination and temporal order judgment.

Visual theory

The visual theory represents a traditional perspective of dyslexia, as being the result of a visual impairment creating problems when processing information from letters and words from a written text. This includes visual processing problems such as binocular, poor vergence, and visual crowding. The Visual Theory does not deny the possibility of alternative causes of dyslexia

# Perceptual noise exclusion hypothesis

The concept of a **perceptual noise exclusion deficit** is an emerging hypothesis as to the origins and nature of dyslexia. It is supported by research showing that dyslexic adults and children experience difficulty in targeting visual information in the presence of visual perceptual distractions, but subjects do not show the same impairment when the distracting factors are removed in an experimental setting. Thus, some dyslexic symptoms appear to arise because of an impaired ability to filter out environmental distractions, and to categorize information so as to distinguish the important sensory data from the irrelevant.

The new research shows that differences in processing ability between dyslexic and non-dyslexic subjects for visual data occurs only in when there are environmental distractions. When the visual distractions were removed, the dyslexic subjects showed no sign of impairment. Further, exposure to external visual noise produced the same level of impairment in dyslexic subjects regardless of the speed of the task being tested.

The researchers have also found that dyslexic children and adults have difficulty forming perceptual categories, such as those involved in distinguishing printed letters and speech sounds, or in deducing rules for sorting of geometrical shapes. This difficulty appears to be closely related to the difficulty with filtering ambient data and focusing on relevant factors while disregarding irrelevant distractors. External noise interferes with the ability of dyslexic subjects to recognize patterns; the lack of a pattern-based template for

interpretation of sensory information in turn may make it difficult to judge the relative importance and relevancy of details as they are perceived.

This hypothesis is supported by a study showing dyslexic subjects in comparison to nondyslexic subjects in the research sample were less responsive to cueing in a visual discrimination task, suggesting that the dyslexics had greater difficulty than controls with prioritizing certain visual information based on previous exposure. The researchers also found that performance on the cuing task could be a more accurate means of discerning dyslexic from normal readers in comparison to the range of other psychophysical tasks typically used in dyslexia research.

# Chapter 8

# Orthographies and Dyslexia

The complexity of a language's orthography, or writing system, can be a significant contributing factor to the difficulties experienced by dyslexic readers. Current psycholinguistic models of dyslexia are "largely developed on the basis of alphabetic writing systems such as English", but the amount of research on some logographic orthographies, Chinese in particular, is also fairly significant. However, little research has been done on syllabic writing systems, and "cross-linguistic studies of the acquired dyslexias and dysgraphias are scarce."

## *Dyslexia and orthographic features*

### The effects of orthographic depth on dyslexia

The complexity of a language's orthography is directly related to the difficulty of learning to read it. Orthographic complexity also contributes to how dyslexia manifests in readers of different languages.

Deep orthographies are writing systems, such as those of English and Arabic, that do not have a one-to-one correspondence between sounds (phonemes) and the letters (graphemes) that represent them. Shallow orthographies have a one-to-one relationship between graphemes and phonemes, and the spelling of words is very consistent.

For languages with more shallow orthographies, such as Italian and Finnish, new readers have few problems learning to decode words. As a result, children learn to read relatively quickly. Most dyslexic readers of shallow orthographies learn to decode words with relative ease, but they tend to have more difficulty with reading fluency and comprehension. The hallmark symptom of dyslexia in a shallow orthography is speed of rapid automatized naming.

For languages with relatively deep orthographies, such as English and French, new readers have a great deal more difficulty learning to decode words. As a result, children learn to read more slowly. Research has shown that the hallmark symptoms of dyslexia in a deep orthography are a deficit in phonological awareness and difficulty reading at the word level. For these dyslexic readers, learning to decode words may take a long time—indeed, in the deepest orthographies the hallmark symptom of dyslexia is the inability to

read at the word level—but many dyslexic readers have relatively fewer problems with fluency and comprehension once some level of decoding has been mastered.

Studies between German and English have shown that the greater depth of English orthography had a "marked adverse effect on reading skills" among dyslexic children.

## *Dyslexia in different types of orthography*

There are a number of different types of writing systems, or orthographies, and they do not necessarily depend on the same neurological skill sets. As a result, certain dyslexic deficits may be more pronounced in some orthographies than in others. For example, in alphabetic languages, phonological awareness is highly predictive of reading ability. But in Chinese (a logographic system), orthographic awareness and motor programming are highly predictive of reading ability.

| Type | Each symbol represents | Example | Predictive skill |
|---|---|---|---|
| Logographic | word or morpheme | Chinese characters | Orthographic awareness, motor programming, naming speed |
| Syllabic | syllable | Japanese *kana* | |
| Alphabetic | phoneme (consonant or vowel) | Latin alphabet | Phonological awareness, naming speed |
| Abugida | phoneme (consonant+vowel) | Indian *Devanāgarī* | Unknown |
| Abjad | phoneme (consonant) | Arabic alphabet | Unknown |
| Featural | phonetic feature | Korean *hangul* | Unknown |

### Dyslexia in alphabetic orthographies

Most of the current research on dyslexia focuses on alphabetic orthography.

Alphabetic writing systems vary significantly in the depth of their orthography. English and French are considered deep orthographies in comparison to Spanish and Italian which are shallow orthographies.

No alphabetic orthography is perfectly phonological; the writing systems of all alphabetic languages vary from this ideal to a greater or lesser extent.

### Dyslexia in logographic orthographies

Most research for logographic orthographies has been done for Chinese. Very little information is available for other logographic orthographies and their relationship to dyslexia.

Logographic writing systems (such as Chinese characters and Cuneiform) are significantly different from alphabetic ones. The primary difference is that their basic graphemes are logograms, a representation based on meaning (morphemes), rather than sounds (phonemes). In some logographic writing systems each character represents a single syllable; in others, each character represents a whole word.

## Chinese orthographies

In alphabetic languages, phonological awareness plays a central role in reading acquisition; in Chinese, phonological awareness is much less important. Rather, reading in Chinese is strongly related to a child's writing skills, which is dependent on orthographic awareness and motor memory. In alphabetic languages with deep orthographies, the difficulty is that the child must cope with having more than one spelling to represent a sound. In spoken Chinese, a single syllable is used in many different words, and a Chinese child must cope with having many written characters that represent the same syllable.

Further complicating the Chinese writing system is that the Chinese character is made up of strokes and sub-character components, substantially increasing visual complexity. Thus, orthographic processing is an important aspect of reading. Deficient orthography-to-meaning mapping can lead to reading disability. A key strategy in teaching children to read is to have children repeatedly write samples of single characters, thus building the child's awareness of a character's internal structure (orthographic awareness).

Rapid naming is one of the best single predictors of dyslexia in all languages tested, including both alphabetic and character-based writing systems. There is some evidence that the means of deciphering characters differs between logographic and alphabetic writing systems differ in the brain: logographic systems echo map-reading skills.

## Dyslexia in syllabic orthographies

A syllabary is a set of written symbols that represent (or approximate) syllables, which make up words. A symbol in a syllabary typically represents an optional consonant sound followed by a vowel sound.

# Chapter 9

# Developmental Dyspraxia

| Developmental dyspraxia | |
|---|---|
| **ICD-10** | F82. |
| **ICD-9** | 315.4 |
| **MeSH** | D001072 |

**Developmental dyspraxia** is a motor learning difficulty that can affect planning of movements and co-ordination as a result of brain messages not being accurately transmitted to the body. It may be diagnosed in the absence of other motor or sensory impairments like cerebral palsy, muscular dystrophy, multiple sclerosis or Parkinson's disease.

## *Terminology*

Dyspraxia is a specific learning difficulty (SpLD) so it does not affect overall intelligence or ability, but just affects particular aspects of development. The concept of developmental dyspraxia has existed for more than a century, but differing interpretations of the terminology remains.

The Dyspraxia Foundation defines developmental dyspraxia as "an impairment or immaturity of the organisation of movement. It is an immaturity in the way that the brain processes information, which results in messages not being properly or fully transmitted. The term dyspraxia comes from the word praxis, which means 'doing, acting'. Dyspraxia affects the planning of what to do and how to do it. It is associated with problems of perception, language and thought". Dyspraxia is described as having two main elements:

- Ideational dyspraxia: difficulty with planning a sequence of coordinated movements.
- Ideo-Motor dyspraxia: difficulty with executing a plan, even though it is known.

Ripley, Daines, and Barrett state that "Developmental dyspraxia is difficulty getting our bodies to do what we want when we want them to do it", and that this difficulty can be considered significant when it interferes with the normal range of activities expected for a

child of their age. The word "dyspraxia" comes from the Greek words "dys" meaning impaired or abnormal and "praxis", meaning action or deed.

## *Epidemiology*

Developmental dyspraxia (referred to as developmental coordination disorder (DCD) in the US and Europe) is a life-long condition that is more common in males than in females, with a ratio of approximately four males to every female. The exact proportion of people with the disorder is unknown since the disorder can be difficult to detect due to a lack of specific laboratory tests, thus making diagnosis of the condition one of elimination of all other possible causes/diseases. Current estimates range from 5%–20% with 5–6% being the most frequently quoted percentage in literature.

## *Assessment and diagnosis*

Assessments for dyspraxia typically require a developmental history, detailing ages at which significant developmental milestones, such as crawling and walking, occurred. Motor skills screening includes activities designed to indicate dyspraxia, including balancing, physical sequencing, touch sensitivity, and variations on walking activities. A baseline motor assessment establishes the starting point for developmental intervention programs. Comparing children to normal rates of development may help to establish areas of significant difficulty.

However, research in the BJSE has shown that knowledge is severely limited in many who should be trained to recognise and respond to various difficulties, including Developmental Coordination Disorder, Dyslexia and DAMP. The earlier that difficulties are noted and timely assessments occur, the quicker intervention can begin. A teacher or GP could miss a diagnosis if they are only applying a cursory knowledge.

"Teachers will not be able to recognise or accommodate the child with learning difficulties in class if their knowledge is limited. Similarly GPs will find it difficult to detect and appropriately refer children with learning difficulties."

## *Developmental profiles*

Various areas of development can be affected by developmental dyspraxia and these will persist into adulthood, as dyspraxia has no cure. Often various coping strategies are developed, and these can be enhanced through occupational therapy, physiotherapy, speech therapy, or psychological training.

### Speech and language

Developmental verbal dyspraxia is a type of ideational dyspraxia, causing linguistic or phonological impairment. This is the favoured term in the UK; however it is also sometimes referred to as articulatory dyspraxia and in the United States the usual term is childhood apraxia of speech (CAS). Key problems include:

- Difficulties controlling the speech organs.
- Difficulties making speech sounds
- Difficulty sequencing sounds
    - Within a word
    - Forming words into sentences
- Difficulty controlling breathing and phonation.
- Slow language development.
- Difficulty with feeding.

## Fine motor control

Difficulties with fine motor co-ordination lead to problems with handwriting, which may be due to either ideational or ideo-motor difficulties. Problems associated with this area may include:

- Learning basic movement patterns.
- Developing a desired writing speed.
- The acquisition of graphemes – e.g. the letters of the Latin alphabet, as well as numbers.
- Establishing the correct pencil grip
- Hand aching while writing

Fine-motor problems can also cause difficulty with a wide variety of other tasks such as using a knife and fork, fastening buttons and shoelaces, cooking, brushing one's teeth, applying cosmetics, styling one's hair, opening jars and packets, locking and unlocking doors, shaving and doing housework.

## Whole body movement, coordination, and body image

Issues with gross motor coordination mean that major developmental targets including walking, running, climbing and jumping can be affected. The difficulties vary from child to child and can include the following:

- Poor timing.
- Poor balance (sometimes even falling over in mid-step). Tripping over one's own feet is also common.
- Difficulty combining movements into a controlled sequence.
- Difficulty remembering the next movement in a sequence.
- Problems with spatial awareness, or proprioception.
- Some people with dyspraxia have trouble picking up and holding onto simple objects such as picking pencils and things up, owing to poor muscle tone and or proprioception.
- This disorder can cause an individual to be clumsy to the point of knocking things over and bumping into people accidentally.
- Some people with dyspraxia have difficulty in determining left from right.

- Cross-laterality, ambidexterity, and a shift in the preferred hand are also common in people with dyspraxia.
- People with dyspraxia may also have trouble determining the distance between them and other objects.

## *General difficulties*

In addition to the physical impairments, dyspraxia is associated with problems with memory, especially short-term memory. This typically results in difficulty remembering instructions, difficulty organizing one's time and remembering deadlines, increased propensity to lose things or problems carrying out tasks which require remembering several steps in sequence (such as cooking.) Whilst most of the general population experience these problems to some extent, they have a much more significant impact on the lives of dyspraxic people. However, many dyspraxics have excellent long-term memories, despite poor short-term memory. Many dyspraxics benefit from working in a structured environment, as repeating the same routine minimises difficulty with time-management and allows them to commit procedures to long-term memory.

People with dyspraxia may have sensory integration dysfunction, including abnormal oversensitivity or undersensitivity to physical stimuli, such as touch, light, and sound. This may manifest itself as an inability to tolerate certain textures such as sandpaper or certain fabrics and including oral toleration of excessively textured food (commonly known as picky eating), or even being touched by another individual (in the case of touch oversensitivity) or may require the consistent use of sunglasses outdoors since sunlight may be intense enough to cause discomfort to a dyspraxic (in the case of light oversensitivity). An aversion to loud music and naturally loud environments (such as clubs and bars) is typical behavior of a dyspraxic individual who suffers from auditory oversensitivity, while only being comfortable in unusually warm or cold environments is typical of a dyspraxic with temperature oversensitivity. Undersensitivity to stimuli may also cause problems. Dyspraxics who are undersensitive to pain may injure themselves without realising. Some dyspraxics may be oversensitive to some stimuli and undersensitive to others. These are commonly associated with autism spectrum conditions.

People with dyspraxia sometimes have difficulty moderating the amount of sensory information that their body is constantly sending them, so as a result these people are prone to panic attacks. Having other autistic traits (which is common with dyspraxia and related conditions) may also contribute to sensory-induced panic attacks.

Dyspraxia can cause problems with perception of distance, and with the speed of moving objects and people This can cause problems moving in crowded places and crossing roads and can make learning to drive a car extremely difficult or impossible.

Many dyspraxics struggle to distinguish left from right, even as adults, and have extremely poor sense of direction generally.

Moderate to extreme difficulty doing physical tasks is experienced by some dyspraxics, and fatigue is common because so much extra energy is expended while trying to execute physical movements correctly. Some (but not all) dyspraxics suffer from hypotonia, which in this case is chronically low muscle tone caused by dyspraxia. People with this condition can have very low muscle strength and endurance (even in comparison with other dyspraxics) and even the simplest physical activities may quickly cause soreness and fatigue, depending on the severity of the hypotonia. Hypotonia may worsen a dyspraxic's already poor balance.

## *Overlap with other conditions*

Dyspraxics may have other difficulties that are not due to dyspraxia itself but often co-exist with it. This is sometimes referred to as comorbidity. Dyspraxics may have characteristics of dyslexia (difficulty with reading and spelling), dyscalculia (difficulty with mathematics), dysgraphia (an inability to write neatly and/or draw) expressive language disorder (difficulty with verbal expression), ADHD (poor attention span and impulsive behaviour), or Asperger syndrome (consisting variously of poor social cognition, a literal understanding of language [making it hard to understand idioms or sarcasm] and rigid, intense interests). However, they are unlikely to have problems in all of these areas. The pattern of difficulty varies widely from person to person, and it is important to understand that a major weakness for one dyspraxic can be a strength or gift for another. For example, while some dyspraxics have difficulty with reading and spelling due to an overlap with dyslexia, or numeracy due to an overlap with dyscalculia, others may have brilliant reading and spelling or mathematical abilities. Similarly, some have autistic traits such as lacking an appreciation of irony or social cues, while others thrive on an ironic sense of humour as a bonding tool and a means of coping.

Students with Dyspraxia struggle most in visual-spatial memory. When compared to their peers who don’t have motor difficulties, students with dyspraxia are seven times more likely than typically developing students to achieve very poor scores in visual-spatial memory. As a result of this working memory impairment, students with dyspraxia have learning deficits as well.

Students with dyspraxia can also have comorbid language impairments (SLI). Research has found that students with dyspraxia and normal language skills still experience learning difficulties despite relative strengths in language. This means that for students with dyspraxia their working memory abilities determine their learning difficulties. Any strength in language that they have is not able to sufficiently support their learning.

## *Other names*

Collier first described developmental dyspraxia as 'congenital maladroitness'. A. Jean Ayres referred to it as a disorder of sensory integration in 1972 while in 1975 Dr Sasson Gubbay called it the 'clumsy child syndrome'. It has also been called minimal brain dysfunction although the two latter names are no longer in use. Other names include:

- Dyspraxia
- Developmental Co-ordination Disorder - a subtly different condition by definition, in practice, very similar.
- Sensorimotor dysfunction
- Perceptuo-motor dysfunction
- Motor Learning Difficulties

The World Health Organisation currently lists Developmental Dyspraxia as Specific Developmental Disorder of Motor Function.

## *Notable dyspraxics*

Living people who have publicly stated they have been diagnosed with dyspraxia include actor Daniel Radcliffe, photographer David Bailey, Florence Welch from Florence and the Machine and actress Hannah McDonnell.

It is difficult to ascertain whether someone now deceased, who was not diagnosed in his/her lifetime, was dyspraxic or not. However, some deceased people suspected to have been dyspraxic include physicist Albert Einstein (although this is subject to some debate, as some have argued that he may have had Asperger's Syndrome, and others speculating that he had both of these conditions).

Writers suspected to have had the condition include Emily Bronte, Charlotte Bronte, poet Samuel Taylor Coleridge, G.K. Chesterton, Ernest Hemingway, Jack Kerouac and George Orwell.

Helen Burns, a character from Charlotte Bronte's *Jane Eyre*, is alleged to have been based on the author's dyspraxic elder sister Maria Bronte.

## Chapter 10

# Dyslexia Research and Management of Dyslexia

# Dyslexia research

Dyslexia is about having problems with a culture's visual notation of speech. The form of the notation varies according to the writing system adopted and developed by each culture. Much of the early **dyslexia research** was based in cultures that adopted a Latin Alphabetic writing systems.

### Dyslexia and language orthography

The Orthography of language has its origins in the Writing Systems developed or adopted by each culture, which varies around the world. There are also orthological differences within each of the main writing systems

### *History of developmental dyslexia*

Dyslexia was first identified by Oswald Berkhan in 1881, and the term 'dyslexia' later coined in 1887 by Rudolf Berlin, an ophthalmologist practicing in Stuttgart, Germany. The history of dyslexia has been the history of Dyslexia research.

### Theories of developmental dyslexia

The theories should not be seen as competing, but viewed as theories trying to explain the underlying causes of a similar set of symptoms from a variety of research perspectives and background.

### Biological dyslexia research

The medical research of dyslexia began with the examination of post autopsy of brains from people who had dyslexia, which lead to the present day genetic research regarding Dyslexia. The parallel evolution of both the theories of dyslexia and the brain scan technology inspired the current interest in researching the Cognitive Neurological causes of dyslexia.

## *Controversy*

Some disagreement exists as to whether dyslexia does indeed exist as a condition, or whether it simply reflects individual differences among different readers.

*The Dyslexia Myth* is a documentary that appeared as part of the *Dispatches* series produced by British broadcaster Channel 4. First aired in September 2005, it claims to expose myths and misconceptions that surround dyslexia. It argues that the common understanding of dyslexia is not only false but makes it more difficult to provide the reading help that hundreds of thousands of children desperately need. Drawing on years of intensive academic research on both sides of the Atlantic, it challenged the existence of dyslexia as a separate condition, and highlighted the many different forms of reading styles. The documentary focused only on the reading difficulties that people with dyslexia encounter, whereas dyslexia has been argued to include symptoms that extend beyond reading difficulties.

Julian Elliot, an educational psychologist at Durham University in the United Kingdom, disputes the characterization of dyslexia as a medical condition, and believes it should be treated simply as a reading difficulty. According to Elliot, "Parents don't want their child to be considered lazy, thick or stupid. If they get called this medically diagnosed term, dyslexic, then it is a signal to all that it's not to do with intelligence." Elliot believes that children of all levels of intelligence may struggle with learning to read, and that all can be helped by educational strategies appropriate to their needs. He feels that resources are wasted on diagnosis and testing, and favors early intervention programs for all struggling readers. More recently Julian Elliot has also made reference to the 28 Definitions of Dyslexia which were documented in the Appendices of the National Research and Development Centre for Adult Literacy and Numeracy report on Developmental dyslexia in adults: a research review by Michael Rice with Greg Brooks May 2004.

John Everatt of the University of Surrey 2007, has suggested that:-

- dyslexic students can be distinguished from other children with low reading achievement by testing geared to assessing their strengths as well as weaknesses
- dyslexic children tend to score significantly better than other children, including non-impaired children, on tests of creativity, spatial memory, and spatial reasoning
- dyslexic children also perform better than other reading-impaired children on tests of vocabulary and listening comprehension
- dyslexic children may be better served by educational intervention which includes strategies geared to their unique strengths in addition to skill remediation

# Management of dyslexia

Managing Dyslexia depends on a multiple of variables, there is no one specific strategy or set of strategies which will work for all who have dyslexia

| Variable | Differences |
|---|---|
| Writing System | Orthography |
| Orthography | Neurological skills |
| Neurological Abilities | Weaknesses and Deficits |
| Neurological Abilities | Strengths |
| Support Provision | National |
| National | Statutory Provisions |
| National | Support Structures |

One factor that characterises the field of dyslexia remediation is the stream of alternative therapies for developmental and learning disabilities. These controversial treatments include nutritional supplements, special diets, homeopathy, and osteopathy/chiropractic manipulation.

## *Writing systems and orthography*

A writing system is a type of symbolic system used to represent elements or statements expressible in language. The orthography of a language specifies the correct way of using a specific writing system to write the language. Where more than one writing system is used for a language, for example for Kurdish, there can be more than one orthography.

### Managing dyslexia when using an alphabetic orthography

Most teaching is geared to remediating specific areas of weakness, such as addressing difficulties with phonetic decoding by providing phonics-based tutoring. Some teaching is geared to specific reading skill areas, such as phonetic decoding; whereas other approaches are more comprehensive in scope, combining techniques to address basic skills along with strategies to improve comprehension and literary appreciation. Many programs are multisensory in design, meaning that instruction includes visual, auditory, and kinesthetic or tactile elements; as it is generally believed that such forms of instruction are more effective for dyslexic learners. Despite claims of some programs to be "research based", there is very little empirical or quantitative research supporting the use of any particular approach to reading instruction as compared to another when used with dyslexic children.

Torgesen (2004) emphasized the importance of explicit instruction for remediation as well as the need for intensity that is completely different from regular classroom instruction. To make gains in reading, students need highly structured, sequential

interactive activities and close monitoring, directly connecting the known with the new, with sufficient time for practice of new skills to build automaticity and fluency. The size of the instructional group is also important, ideally between 1:1 and 1:3.

## *National statutory provision and support structures*

Each country has adopted and developed a writing system of choice. Each country has their own Statutes relating to the provision of Education, and special educational needs. The statutory provision framework of support in each country is usually complemented by many independent and voluntary support agencies providing more specialised information and support.

# Chapter 11

# Alternative Therapies for Developmental and Learning Disabilities

**Alternative therapies for developmental and learning disabilities** include a range of practices used in the treatment of dyslexia, ADHD, Asperger syndrome, autism, Down syndrome and other developmental and learning disabilities. Treatments include changes in diet, dietary supplements, biofeedback, chelation therapy, homeopathy, massage and yoga. These therapies generally rely on theories that have little scientific basis, lacking well-controlled, large, randomized trials to demonstrate safety and efficacy; small trials that have reported beneficial effects can be generally explained by the ordinary waxing and waning of the underlying conditions.

## *Treatment needs*

There are a number of non-standard treatments for developmental and learning disabilities. There is a call for alternative therapies particularly when a condition lacks a reliable remediation. For example, there is no cure for autism; the main goals of mainstream behavioral and medical management are to lessen associated deficits and family distress, and to increase quality of life and functional independence. Some alternative therapies, such as gluten-free, casein-free diets, may be appealing to some parents because the treatment recommended by most experts is thought to be "cold and manipulative". Parents may also consider a drug treatment for attention deficit as avoidable. Alternative treatments to a stimulant medication range from natural products to psychotherapeutic techniques and highly technological interventions. It has been argued that although texts that promote alternative therapies do not directly accuse parents of inadequacy, the claims that the disability is caused by certain factors, such as poor nutrition, supports the culture of mother-blame.

## *Prevalence*

From 12% to 64% of families of a child with ADHD use an alternative therapy, with the lower estimates likely come from narrower definitions of complementary and alternative medicine (CAM). School teachers, family and friends are the most common source of suggestion of alternative therapies for ADHD. In 2003, 64 percent of families of a child with special health care needs reported that they use alternative therapies. These therapies included spiritual healing, massage, chiropractic, herbs and special diets, homeopathy,

self hypnosis and other methods of complementary and alternative medicine. The need for an alternative therapy was related to the child's condition and to its evaluation as repairable or not. A 2008 study found that about 40% of Hong Kong children with autism spectrum disorder were treated with CAM, with the most popular therapies being acupuncture, sensory integration therapy, and Chinese herbology; the 40% is a lower prevalence than in Canada and the U.S., where biological-based therapies such as special diets predominate. In the U.S. CAM is used by an estimated 20–40% of healthy children, 30–70% of children with special health care needs, and 52–95% of children with autism, and a 2009 survey of U.S. primary care physicians found that more of them recommended than discouraged multivitamins, essential fatty acids, melatonin, and probiotics as CAM treatments for autism.

## *Evidence basis*

Complementary and alternative medicine often lacks support in scientific evidence, so its safety and efficacy are often questionable. Some therapists who advocate CAM may claim to cure many conditions or disabilities that are not diseases and therefore cannot be "cured".

While some experts encourage parents to be open-minded, others argue that treatments and services with no proven efficacy have *opportunity costs* because they displace the opportunity to participate in efficient treatments and services. According to Scott O. Lilienfeld,

many individuals who spend large amounts of time and money on ineffective treatments may be left with precious little of either. As a result, they may forfeit the opportunity to obtain treatments that could be more helpful. Thus, even ineffective treatments that are by themselves innocuous can indirectly produce negative consequences.

There is often little or no scientific evidence for effectiveness of alternative therapies. It may be difficult to separate the success of a specific treatment from natural development or from the benefits of the individual's positive attitude. Some phenomena to be considered when evaluating studies are the placebo effect, the Hawthorne effect and different types of attentional and motivational effects. Doubtless, people with disabilities may benefit from some alternative therapies, at least for relaxation, social interaction, personal development and self-esteem. This can be important because many children with learning difficulties suffer from low self-esteem.

For instance, a randomised controlled trial with dyslexic children was undertaken to evaluate the efficiency of Sunflower therapy which includes applied kinesiology, physical manipulation, massage, homeopathy, herbal remedies and neuro-linguistic programming. There were no significant improvements in cognitive nor literacy test performance associated with the treatment, but there were significant improvements in self-esteem for the treatment group. This study did not control for the placebo effect.

## *Precautions*

Because many alternative therapies have not been evaluated in scientific studies there may be no guarantee for their safety. In most countries, with the exception of osteopathy and chiropractic, complementary medical disciplines have not been state registered. This means there is no law to forbid anyone from setting up as a practitioner even with no qualification nor experience. There are also a lot of 'universities' offering all kinds of alternative medicine degrees for a fee, and their certificates can look very real. These organisations may, on the other hand, offer ongoing training and an insurance to their registered members.

Experts of alternative therapies advise customers to be careful when choosing a therapist. Before taking a therapy, it is wise to find out whether or not previous customers recommend it, the therapist has a qualification and is a registered practitioner, whether the therapy could be dangerous, how much the treatment costs, and whether money will be refunded if the therapy does not work.

# Chapter 12

# Attention Deficit Hyperactivity Disorder

## Attention-deficit/hyperactivity disorder

A child not paying attention in class.

| | |
|---|---|
| **ICD-10** | F90. |
| **ICD-9** | 314.00, 314.01 |
| **OMIM** | 143465 |
| **DiseasesDB** | 6158 |
| **MedlinePlus** | 001551 |
| **eMedicine** | med/3103 ped/177 |
| **MeSH** | D001289 |

**Attention deficit hyperactivity disorder** (**ADHD** or **AD/HD** or **ADD**) is a neurobehavioral developmental disorder. It is primarily characterized by "the co-existence of attentional problems and hyperactivity, with each behavior occurring infrequently alone" and symptoms starting before seven years of age.

ADHD is the most commonly studied and diagnosed psychiatric disorder in children, affecting about 3 to 5 percent of children globally and diagnosed in about 2 to 16 percent of school aged children. It is a chronic disorder with 30 to 50 percent of those individuals diagnosed in childhood continuing to have symptoms into adulthood. Adolescents and adults with ADHD tend to develop coping mechanisms to compensate for some or all of their impairments. It is estimated that 4.7 percent of American adults live with ADHD.

ADHD is diagnosed two to four times more frequently in boys than in girls, though studies suggest this discrepancy may be partially due to subjective bias of referring

teachers. ADHD management usually involves some combination of medications, behavior modifications, lifestyle changes, and counseling. Its symptoms can be difficult to differentiate from other disorders, increasing the likelihood that the diagnosis of ADHD will be missed. Additionally, most clinicians have not received formal training in the assessment and treatment of ADHD, particularly in adult patients.

ADHD and its diagnosis and treatment have been considered controversial since the 1970s. The controversies have involved clinicians, teachers, policymakers, parents and the media. Topics include the actuality of the disorder, its causes, and the use of stimulant medications in its treatment. Most healthcare providers accept that ADHD is a genuine disorder with debate in the scientific community centering mainly around how it is diagnosed and treated. The American Medical Association concluded in 1998 that the diagnostic criteria for ADHD are based on extensive research and, if applied appropriately, lead to the diagnosis with high reliability.

## *Classification*

ADHD may be seen as one or more continuous traits found normally throughout the general population. It is a developmental disorder in which certain traits such as impulse control lag in development. Using magnetic resonance imaging of the prefrontal cortex, this developmental lag has been estimated to range from 3 to 5 years. A diagnosis of ADHD does not, however, imply a neurological disease. ADHD is classified as a disruptive behavior disorder along with oppositional defiant disorder, conduct disorder and antisocial disorder.

ADHD has three subtypes:

- Predominantly hyperactive-impulsive
    - Most symptoms (six or more) are in the hyperactivity-impulsivity categories.
    - Fewer than six symptoms of inattention are present, although inattention may still be present to some degree.
- Predominantly inattentive
    - The majority of symptoms (six or more) are in the inattention category and fewer than six symptoms of hyperactivity-impulsivity are present, although hyperactivity-impulsivity may still be present to some degree.
    - Children with this subtype are less likely to act out or have difficulties getting along with other children. They may sit quietly, but they are not paying attention to what they are doing. Therefore, the child may be overlooked, and parents and teachers may not notice symptoms of ADHD.
- Combined hyperactive-impulsive and inattentive
    - Six or more symptoms of inattention and six or more symptoms of hyperactivity-impulsivity are present.
    - Most children with ADHD have the combined type.

## *Signs and symptoms*

Inattention, hyperactivity, and impulsivity are the key behaviors of ADHD. The symptoms of ADHD are especially difficult to define because it is hard to draw the line at where normal levels of inattention, hyperactivity, and impulsivity end and clinically significant levels requiring intervention begin. To be diagnosed with ADHD, symptoms must be observed in two different settings for six months or more and to a degree that is greater than other children of the same age.

The symptom categories of ADHD in children yield three potential classifications of ADHD—predominantly inattentive type, predominantly hyperactive-impulsive type, or combined type if criteria for both subtypes are met:[:p.4]

Predominantly inattentive type symptoms may include:

- Be easily distracted, miss details, forget things, and frequently switch from one activity to another
- Have difficulty maintaining focus on one task
- Become bored with a task after only a few minutes, unless doing something enjoyable
- Have difficulty focusing attention on organizing and completing a task or learning something new or trouble completing or turning in homework assignments, often losing things (e.g., pencils, toys, assignments) needed to complete tasks or activities
- Not seem to listen when spoken to
- Daydream, become easily confused, and move slowly
- Have difficulty processing information as quickly and accurately as others
- Struggle to follow instructions.

Predominantly hyperactive-impulsive type symptoms may include:

- Fidget and squirm in their seats
- Talk nonstop
- Dash around, touching or playing with anything and everything in sight
- Have trouble sitting still during dinner, school, and story time
- Be constantly in motion
- Have difficulty doing quiet tasks or activities.

and also these manifestations primarily of impulsivity:

- Be very impatient
- Blurt out inappropriate comments, show their emotions without restraint, and act without regard for consequences
- Have difficulty waiting for things they want or waiting their turns in games

Most people exhibit some of these behaviors, but not to the degree where such behaviors significantly interfere with a person's work, relationships, or studies. The core impairments are consistent even in different cultural contexts.

Symptoms may persist into adulthood for up to half of children diagnosed with ADHD. Estimating this is difficult as there are no official diagnostic criteria for ADHD in adults. ADHD in adults remains a clinical diagnosis. The signs and symptoms may differ from those during childhood and adolescence due to the adaptive processes and avoidance mechanisms learned during the process of socialisation.

A 2009 study found that children with ADHD move around a lot because it helps them stay alert enough to complete challenging tasks.

## Comorbid disorders

ADHD may accompany other disorders such as anxiety or depression. Such combinations can greatly complicate diagnosis and treatment. Academic studies and research in private practice suggest that depression in ADHD appears to be increasingly prevalent in children as they get older, with a higher rate of increase in girls than in boys, and to vary in prevalence with the subtype of ADHD. Where a mood disorder complicates ADHD it would be prudent to treat the mood disorder first, but parents of children who have ADHD often wish to have the ADHD treated first, because the response to treatment is quicker.

Inattention and "hyperactive" behavior are not the only problems in children with ADHD. ADHD exists alone in only about 1/3 of the children diagnosed with it. Many co-existing conditions require other courses of treatment and should be diagnosed separately instead of being grouped in the ADHD diagnosis. Some of the associated conditions are:

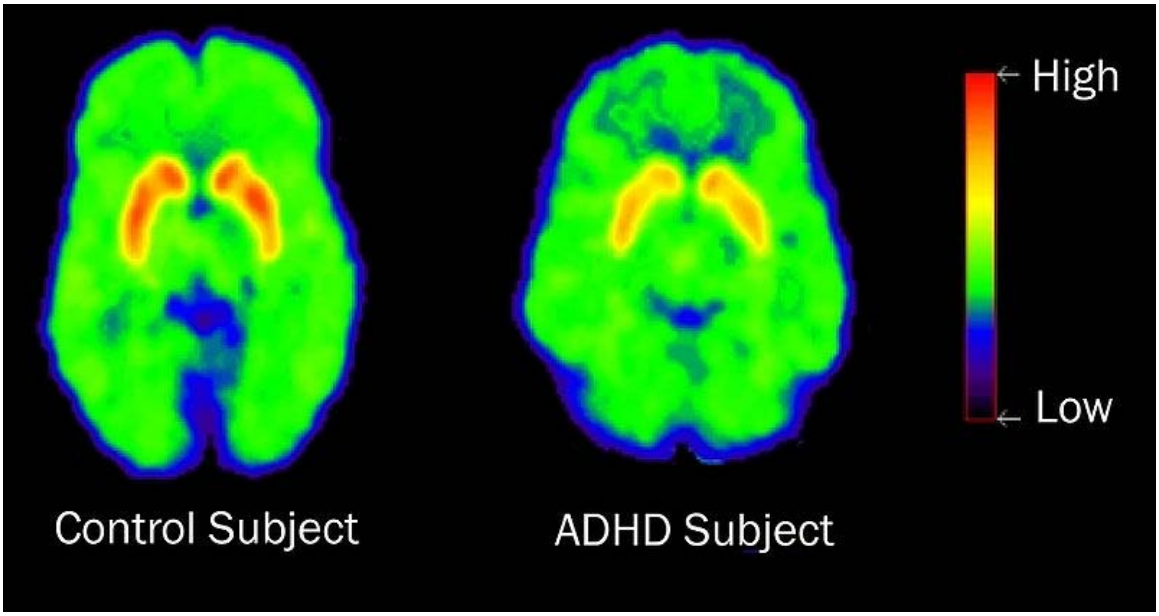
- Oppositional defiant disorder (35%) and conduct disorder (26%) which both are characterized by antisocial behaviors such as stubbornness, aggression, frequent temper tantrums, deceitfulness, lying, or stealing, inevitably linking these comorbid disorders with antisocial personality disorder (ASPD); about half of those with hyperactivity and ODD or CD develop ASPD in adulthood.
- Borderline personality disorder, which was according to a study on 120 female psychiatric patients diagnosed and treated for BPD associated with ADHD in 70 percent of those cases.
- Primary disorder of vigilance, which is characterized by poor attention and concentration, as well as difficulties staying awake. These children tend to fidget, yawn and stretch and appear to be hyperactive in order to remain alert and active.
- Mood disorders. Boys diagnosed with the combined subtype have been shown likely to suffer from a mood disorder.
- Bipolar disorder. As many as 25 percent of children with ADHD have bipolar disorder. Children with this combination may demonstrate more aggression and behavioral problems than those with ADHD alone.

- Anxiety disorder, which has been found to be common in girls diagnosed with the inattentive subtype of ADHD.
- Obsessive-compulsive disorder. OCD is believed to share a genetic component with ADHD and shares many of its characteristics.

## *Cause*

The specific causes of ADHD are not known. There are, however, a number of factors that may contribute to, or exacerbate ADHD. They include genetics, diet and the social and physical environments.

### Genetics




PET scan: ADHD brains dopamine transporters

Twin studies indicate that the disorder is highly heritable and that genetics are a factor in about 75 percent of all cases. Hyperactivity also seems to be primarily a genetic condition; however, other causes do have an effect.

Researchers believe that a large majority of ADHD cases arise from a combination of various genes, many of which affect dopamine transporters. Candidate genes include $\alpha_{2A}$ adrenergic receptor, dopamine transporter, dopamine receptors $D_2/D_3$, dopamine beta-hydroxylase monoamine oxidase A, catecholamine-methyl transferase, serotonin transporter promoter (SLC6A4), $5HT_{2A}$ receptor, $5HT_{1B}$ receptor, the 10-repeat allele of the DAT1 gene, the 7-repeat allele of the DRD4 gene, and the dopamine beta hydroxylase gene (DBH TaqI). A common variant of a gene called LPHN3 is estimated to be responsible for about 9% of the incidence of ADHD, and ADHD cases where this gene is present are particularly responsive to stimulant medication.

The broad selection of targets indicates that ADHD does not follow the traditional model of "a simple genetic disease" and should therefore be viewed as a complex interaction among genetic and environmental factors. Even though all these genes might play a role, to date no single gene has been shown to make a major contribution to ADHD.

## Evolutionary theories

The hunter vs. farmer theory is a hypothesis proposed by author Thom Hartmann about the origins of ADHD. The theory proposes that hyperactivity may be an adaptive behavior in pre-modern humans and that those with ADHD retain some of the older "hunter" characteristics associated with early pre-agricultural human society. According to this theory, individuals with ADHD may be more adept at searching and seeking and less adept at staying put and managing complex tasks over time. Further evidence showing hyperactivity may be evolutionarily beneficial was put forth in 2006 in a study which found it may carry specific benefits for certain forms of ancient society. In these societies, those with ADHD are hypothesized to have been more proficient in tasks involving risk or competition (i.e. hunting, mating rituals, etc.). A genetic variant associated with ADHD (DRD4 48bp VNTR 7R allele), has been found to be at higher frequency in more nomadic populations and those with more of a history of migration. Consistent with this, another group of researchers observed that the health status of nomadic Ariaal men was higher if they had the ADHD associated genetic variant (7R alleles). However in recently sedentary (non-nomadic) Ariaal those with 7R alleles seemed to have slightly worse health.

## Environmental

Twin studies to date have suggested that approximately 9 to 20 percent of the variance in hyperactive-impulsive-inattentive behavior or ADHD symptoms can be attributed to nonshared environmental (nongenetic) factors. Environmental factors implicated include alcohol and tobacco smoke exposure during pregnancy and environmental exposure to lead in very early life. The relation of smoking to ADHD could be due to nicotine causing hypoxia (lack of oxygen) to the fetus *in utero*. It could also be that women with ADHD are more likely to smoke and therefore, due to the strong genetic component of ADHD, are more likely to have children with ADHD. Complications during pregnancy and birth—including premature birth—might also play a role. ADHD patients have been observed to have higher than average rates of head injuries; however, current evidence does not indicate that head injuries are the cause of ADHD in the patients observed. Infections during pregnancy, at birth, and in early childhood are linked to an increased risk of developing ADHD. These include various viruses (measles, varicella, rubella, enterovirus 71) and streptococcal bacterial infection.

A 2007 study linked the organophosphate insecticide chlorpyrifos, which is used on some fruits and vegetables, with delays in learning rates, reduced physical coordination, and behavioral problems in children, especially ADHD.

A 2010 study found that pesticide exposure is strongly associated with an increased risk of ADHD in children. Researchers analyzed the levels of organophosphate residues in the urine of more than 1,100 children aged 8 to 15 years old, and found that those with the highest levels of dialkyl phosphates, which are the breakdown products of organophosphate pesticides, also had the highest incidence of ADHD. Overall, they found a 35 percent increase in the odds of developing ADHD with every 10-fold increase in urinary concentration of the pesticide residues. The effect was seen even at the low end of exposure: children who had any detectable, above-average level of pesticide metabolite in their urine were twice as likely as those with undetectable levels to record symptoms of ADHD.

## Diet

A study published in The Lancet in 2007 found a link between children's ingestion of many commonly used artificial food colors, the preservative sodium benzoate and hyperactivity. In response to these findings, the British government took prompt action. According to the Food Standards Agency, the food regulatory agency in the UK, food manufacturers are being encouraged to voluntarily phase out the use of most artificial food colors by the end of 2009. Following the FSA's actions, the European Commission ruled that any food products containing the "Southampton Six" (The contentious colourings are: sunset yellow FCF (E110), quinoline yellow (E104), carmoisine (E122), allura red (E129), tartrazine (E102) and ponceau 4R (E124)) must display warning labels on their packaging by 2010. In the US, little has been done to curb food manufacturer's use of specific food colors, despite the new evidence presented by the Southampton study. However, the existing US Food Drug and Cosmetic Act had already required that artificial food colors be approved for use, that they must be given FD&C numbers by the FDA, and the use of these colors must be indicated on the package. This is why food packaging in the USA may state something like: "Contains FD&C Red #40."

## Social

The World Health Organization states that the diagnosis of ADHD can represent family dysfunction or inadequacies in the educational system rather than individual psychopathology. Other researchers believe that relationships with caregivers have a profound effect on attentional and self-regulatory abilities. A study of foster children found that a high number of them had symptoms closely resembling ADHD. Researchers have found behavior typical of ADHD in children who have suffered violence and emotional abuse. Furthermore, Complex Post Traumatic Stress Disorder can result in attention problems that can look like ADHD. ADHD is also considered to be related to sensory integration dysfunction.

A 2010 article by CNN suggests that there is an increased risk for internationally adopted children to develop mental health disorders, such as ADHD and ODD. The risk may be related to the length of time the children spent in an orphanage, especially if they were neglected or abused. Many of these families who adopted the affected children feel overwhelmed and frustrated, since managing their children may entail more

responsibilities than originally anticipated. The adoption agencies may be aware of the child's behavioral history, but decide to withhold the information prior to the adoption. This in turn has resulted in some parents suing adoption agencies, the abuse of children, and even the relinquishment of the child.

## Neurodiversity

Proponents of the neurodiversity theory assert that atypical (neurodivergent) neurological development is a normal human difference that is to be tolerated and respected just like any other human difference. Social critics argue that while biological factors may play a large role in difficulties with sitting still in class and/or concentrating on schoolwork in some children, these children could have failed to integrate others' social expectations of their behavior for a variety of other reasons. As genetic research into ADHD proceeds, it may become possible to integrate this information with the neurobiology in order to distinguish disability from varieties of normal or even exceptional functioning in people along the same spectrum of attention differences.

## Social construct theory of ADHD

Social construction theory states that it is societies that determine where the line between normal and abnormal behavior is drawn. Thus society members including physicians, parents, teachers, and others are the ones who determine which diagnostic criteria are applied and thus determine the number of people affected. This is exemplified in the fact that the DSM IV arrives at levels of ADHD three to four times higher than those obtained with use of the ICD 10. Thomas Szasz, an extreme proponent of this theory, has gone so far as to state that ADHD was "invented and not discovered."

## Low arousal theory

According to the low arousal theory, people with ADHD need excessive activity as self-stimulation because of their state of abnormally low arousal. The theory states that those with ADHD cannot self-moderate, and their attention can only be gained by means of environmental stimuli, which in turn results in disruption of attentional capacity and an increase in hyperactive behaviour.

Without enough stimulation coming from the environment, an ADHD child will create it him or herself by walking around, fidgeting, talking, etc. This theory also explains why stimulant medications have high success rates and can induce a calming effect at therapeutic dosages among children with ADHD. It establishes a strong link with scientific data that ADHD is connected to abnormalities with the neurochemical dopamine and a powerful link with low-stimulation PET scan results in ADHD subjects.

## *Pathophysiology*

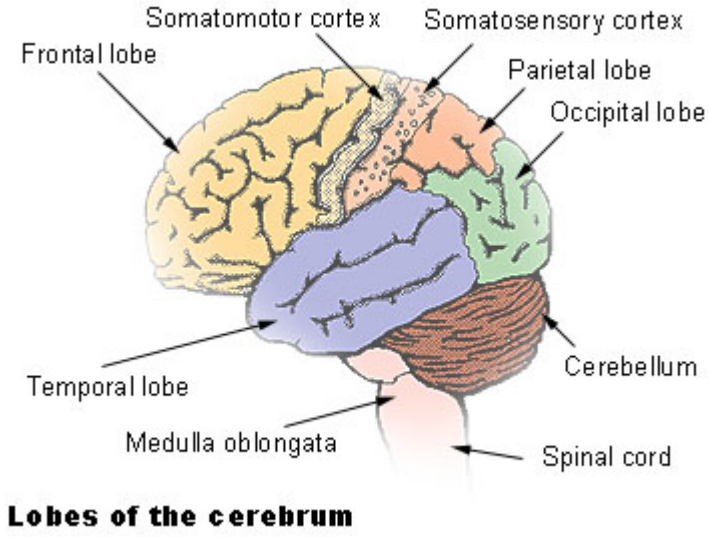



Diagram of the human brain

The pathophysiology of ADHD is unclear and there are a number of competing theories. Research on children with ADHD has shown a general reduction of brain volume, but with a proportionally greater reduction in the volume of the left-sided prefrontal cortex. These findings suggest that the core ADHD features of inattention, hyperactivity, and impulsivity may reflect frontal lobe dysfunction, but other brain regions particularly the cerebellum have also been implicated. Neuroimaging studies in ADHD have not always given consistent results and as of 2008 are only used for research not diagnostic purposes. A 2005 review of published studies involving neuroimaging, neuropsychological genetics, and neurochemistry found converging lines of evidence to suggest that four connected frontostriatal regions play a role in the pathophysiology of ADHD: The lateral prefrontal cortex, dorsal anterior cingulate cortex, caudate, and putamen.

In one study a delay in development of certain brain structures by an average of three years occurred in ADHD elementary school aged patients. The delay was most prominent in the frontal cortex and temporal lobe, which are believed to be responsible for the ability to control and focus thinking. In contrast, the motor cortex in the ADHD patients was seen to mature faster than normal, suggesting that both slower development of behavioral control and advanced motor development might be required for the fidgetiness that characterizes ADHD. It should be noted that stimulant medication itself may affect growth factors of the central nervous system.

The same laboratory had previously found involvement of the "7-repeat" variant of the dopamine D4 receptor gene, which accounts for about 30 percent of the genetic risk for ADHD, in unusual thinness of the cortex of the right side of the brain; however, in contrast to other variants of the gene found in ADHD patients, the region normalized in thickness during the teen years in these children, coinciding with clinical improvement.

Additionally, SPECT scans found people with ADHD to have reduced blood circulation (indicating low neural activity), and a significantly higher concentration of dopamine transporters in the striatum which is in charge of planning ahead. A study by the U.S. Department of Energy's Brookhaven National Laboratory in collaboration with Mount Sinai School of Medicine in New York suggest that it is not the dopamine transporter levels that indicate ADHD, but the brain's ability to produce neurotransmitters like dopamine itself. The study was done by injecting 20 ADHD subjects and 25 control subjects with a radiotracer that attaches itself to dopamine transporters. The study found that it was not the transporter levels that indicated ADHD, but the dopamine itself. ADHD subjects showed lower levels of dopamine (hypodopaminergia) across the board. They speculated that since ADHD subjects had lower levels of dopamine to begin with, the number of transporters in the brain was not the telling factor. In support of this notion, plasma homovanillic acid, an index of dopamine levels, was found to be inversely related not only to childhood ADHD symptoms in adult psychiatric patients, but to "childhood learning problems" in healthy subjects as well. One interpretation of dopamine pathway tracers is that the biochemical "reward" mechanism works for those with ADHD only when the task performed is inherently motivating; low levels of dopamine raise the threshold at which someone can maintain focus on a task which is otherwise boring. Neuroimaging studies also found that neurotransmitters level (e.g. dopamine and serotonin) in the synaptic cleft goes down during depression.

A 1990 PET scan study by Alan J. Zametkin *et al.* found that global cerebral glucose metabolism was 8 percent lower in medication-naive adults who had been hyperactive since childhood. Further studies found that chronic stimulant treatment had little effect on global glucose metabolism, a 1993 study in girls failed to find a decreased global glucose metabolism, but found significant differences in glucose metabolism in 6 specific regions of the brains of ADHD girls as compared to control subjects. The study also found that differences in one specific region of the frontal lobe were statistically correlated with symptom severity. A further study in 1997 also failed to find global differences in glucose metabolism, but similarly found differences in glucose normalization in specific regions of the brain. The 1997 study also noted that their findings were somewhat different than those in the 1993 study, and concluded that sexual maturation may have played a role in this discrepancy. The significance of the research by Zametkin has not been determined and neither his group nor any other has been able to replicate the 1990 results.

Critics, such as Jonathan Leo and David Cohen, who reject the characterization of ADHD as a disorder, contend that the controls for stimulant medication usage were inadequate in some lobar volumetric studies which makes it impossible to determine whether ADHD itself or psychotropic medication used to treat ADHD is responsible for the decreased thickness observed in certain brain regions. While the main study in question used age-matched controls, it did not provide information on height and weight of the subjects. These variables it has been argued could account for the regional brain size differences rather than ADHD itself. They believe many neuroimaging studies are oversimplified in both popular and scientific discourse and given undue weight despite deficiencies in experimental methodology.

## *Diagnosis*

ADHD is diagnosed via a psychiatric assessment; to rule out other potential causes or comorbidities, physical examination, radiological imaging, and laboratory tests may be used.

In North America, the DSM-IV criteria are often the basis for a diagnosis, while European countries usually use the ICD-10. If the DSM-IV criteria are used, rather than the ICD-10, a diagnosis of ADHD is 3–4 times more likely. Factors other than those within the DSM or ICD however have been found to affect the diagnosis in clinical practice. A child's social and school environment as well as academic pressures at school are likely to be of influence.

Many of the symptoms of ADHD occur from time to time in everyone; in patients with ADHD, the frequency of these symptoms is greater and patients' lives are significantly impaired. Impairment must occur in multiple settings to be classified as ADHD. As with many other psychiatric and medical disorders, the formal diagnosis is made by a qualified professional in the field based on a set number of criteria. In the USA these criteria are laid down by the American Psychiatric Association in their Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), 4th edition. Based on the DSM-IV criteria listed below, three types of ADHD are classified:

1. ADHD, Combined Type: if both criteria 1A and 1B are met for the past 6 months
2. ADHD Predominantly Inattentive Type: if criterion 1A is met but criterion 1B is not met for the past six months
3. ADHD, Predominantly Hyperactive-Impulsive Type: if criterion 1B is met but criterion 1A is not met for the past six months.

The previously used term *ADD* expired with the most recent revision of the DSM. Consequently, ADHD is the current nomenclature used to describe the disorder as one distinct disorder which can manifest itself as being a primary deficit resulting in hyperactivity/impulsivity (ADHD, predominately hyperactive-impulsive type) or inattention (ADHD predominately inattentive type) or both (ADHD combined type).

### DSM-IV

IA. Six or more of the following signs of inattention have been present for at least 6 months to a point that is disruptive and inappropriate for developmental level:

- *Inattention:*

1. Often does not give close attention to details or makes careless mistakes in schoolwork, work, or other activities.
2. Often has trouble keeping attention on tasks or play activities.
3. Often does not seem to listen when spoken to directly.

4. Often does not follow instructions and fails to finish schoolwork, chores, or duties in the workplace (not due to oppositional behavior or failure to understand instructions).
5. Often has trouble organizing activities.
6. Often avoids, dislikes, or doesn't want to do things that take a lot of mental effort for a long period of time (such as schoolwork or homework).
7. Often loses things needed for tasks and activities (such as toys, school assignments, pencils, books, or tools).
8. Is often easily distracted.
9. Often forgetful in daily activities.

IB. Six or more of the following signs of hyperactivity-impulsivity have been present for at least 6 months to an extent that is disruptive and inappropriate for developmental level:

- *Hyperactivity:*

1. Often fidgets with hands or feet or squirms in seat.
2. Often gets up from seat when remaining in seat is expected.
3. Often runs about or climbs when and where it is not appropriate (adolescents or adults may feel very restless).
4. Often has trouble playing or enjoying leisure activities quietly.
5. Is often "on the go" or often acts as if "driven by a motor".
6. Often talks excessively.

- *Impulsiveness:*

1. Often blurts out answers before questions have been finished.
2. Often has trouble waiting one's turn.
3. Often interrupts or intrudes on others (example: butts into conversations or games).

II. Some signs that cause impairment were present before age 7 years.

III. Some impairment from the signs is present in two or more settings (such as at school/work and at home).

IV. There must be clear evidence of significant impairment in social, school, or work functioning.

V. The signs do not happen only during the course of a Pervasive Developmental Disorder, Schizophrenia, or other Psychotic Disorder. The signs are not better accounted for by another mental disorder (such as Mood Disorder, Anxiety Disorder, Dissociative Identity Disorder, or a Personality Disorder).

## ICD-10

In the tenth edition of the *International Statistical Classification of Diseases and Related Health Problems* (ICD-10) the signs of ADHD are given the name "Hyperkinetic disorders". When a conduct disorder (as defined by ICD-10) is present, the condition is referred to as "Hyperkinetic conduct disorder". Otherwise the disorder is classified as "Disturbance of Activity and Attention", "Other Hyperkinetic Disorders" or "Hyperkinetic Disorders, Unspecified". The latter is sometimes referred to as, "Hyperkinetic Syndrome".

## Other guidelines

The American Academy of Pediatrics Clinical Practice Guideline for children with ADHD emphasizes that a reliable diagnosis is dependent upon the fulfillment of three criteria:

- The use of explicit criteria for the diagnosis using the DSM-IV-TR.
- The importance of obtaining information about the child's signs in more than one setting.
- The search for coexisting conditions that may make the diagnosis more difficult or complicate treatment planning.

All three criteria are determined using the patient's history given by the parents, teachers and/or the patient.

Adults often continue to be impaired by ADHD. Adults with ADHD are diagnosed under the same criteria, including the stipulation that their signs must have been present prior to the age of seven. Adults face some of their greatest challenges in the areas of self-control and self-motivation, as well as executive functioning, usually having more signs of inattention and fewer of hyperactivity or impulsiveness than children do.

The American Academy of Child Adolescent Psychiatry (AACAP) considers it necessary that the following be present before attaching the label of ADHD to a child:

- The behaviors must appear before age 7.
- They must continue for at least six months.
- The symptoms must also create a real handicap in at least two of the following areas of the child's life:
    - in the classroom,
    - on the playground,
    - at home,
    - in the community, or
    - in social settings.

If a child seems too active on the playground but not elsewhere, the problem might not be ADHD. It might also not be ADHD if the behaviors occur in the classroom but nowhere

else. A child who shows some symptoms would not be diagnosed with ADHD if his or her schoolwork or friendships are not impaired by the behaviors.

## Differential

To make the diagnosis of ADHD, a number of other possible medical and psychological conditions must be excluded.

**Medical conditions**

Medical conditions that must be excluded include: hypothyroidism, anemia, lead poisoning, chronic illness, hearing or vision impairment, substance abuse, medication side effects, sleep impairment and child abuse, and cluttering (tachyphemia) among others.

**Sleep conditions**

As with other psychological and neurological issues, the relationship between ADHD and sleep is complex. In addition to clinical observations, there is substantial empirical evidence from a neuroanatomic standpoint to suggest that there is considerable overlap in the central nervous system centers that regulate sleep and those that regulate attention/arousal. Primary sleep disorders play a role in the clinical presentation of symptoms of inattention and behavioral dysregulation. There are multilevel and bidirectional relationships among sleep, neurobehavioral functioning and the clinical syndrome of ADHD.

Behavioral manifestations of sleepiness in children range from the classic ones (yawning, rubbing eyes), to externalizing behaviors (impulsivity, hyperactivity, aggressiveness), to mood lability and inattentiveness. Many sleep disorders are important causes of symptoms which may overlap with the cardinal symptoms of ADHD; children with ADHD should be regularly and systematically assessed for sleep problems.

From a clinical standpoint, mechanisms that account for the phenomenon of excessive daytime sleepiness include:

- Chronic sleep deprivation, that is insufficient sleep for physiologic sleep needs,
- Fragmented or disrupted sleep, caused by, for example, obstructive sleep apnea (OSA) or periodic limb movement disorder (PLMD),
- Primary clinical disorders of excessive daytime sleepiness, such as narcolepsy and
- Circadian rhythm disorders, such as delayed sleep phase syndrome (DSPS). A study in the Netherlands compared two groups of unmedicated 6-12-year-olds, all of them with "rigorously diagnosed ADHD". 87 of them had problems getting to sleep, 33 had no sleep problems. The larger group had a significantly later dim light melatonin onset (DLMO) than did the children with no sleep problems.

## *Management*

Methods of treatment often involve some combination of behavior modification, life-style changes, counseling, and medication. A 2005 study found that medical management and behavioral treatment is the most effective ADHD management strategy, followed by medication alone, and then behavioral treatment. While medication has been shown to improve behavior when taken over the short term, they have not been shown to alter long term outcomes. Medications have at least some effect in about 80% of people.

### Psychosocial

The evidence is strong for the effectiveness of behavioral treatments in ADHD. It is recommended first line in those who have mild symptoms and in preschool aged children. Psychological therapies used include psychoeducational input, behavior therapy, cognitive behavioral therapy (CBT), interpersonal psychotherapy (IPT), family therapy, school-based interventions, social skills training and parent management training.

Parent training and education have been found to have short term benefits. Family therapy has shown to be of little use in the treatment of ADHD, though it may be worth noting that parents of children with ADHD are more likely to divorce than parents of children without ADHD, particularly when their children are younger than eight years old. Several ADHD specific support groups exist as informational sources and to help families cope with challenges associated with dealing with ADHD.

### Medication

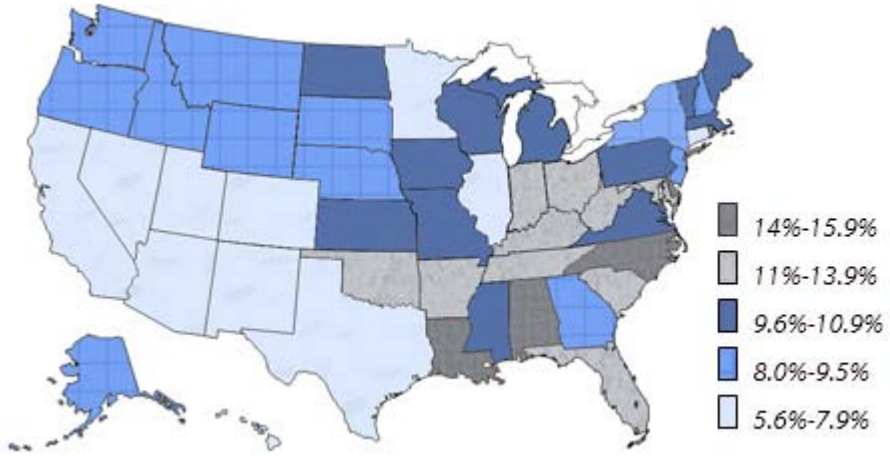

Methylphenidate (Ritalin 10 mg tablets)

Stimulant medication are the medical treatment of choice. There are a number of non-stimulant medications, such as atomoxetine, that may be used as alternatives. There are no good studies of comparative effectiveness between various medications, and there is a lack of evidence on their effects on academic performance and social behaviors. While stimulants and atomoxetine are generally safe, there are side effects and contraindications to their use. Medications are not recommended for preschool children, as their long-term effects in such young people are unknown. There is very little data on the long-term adverse effects or benefits of stimulants for ADHD. Guidelines on when to use medications vary internationally, with the UK's National Institute of Clinical Excellence, for example, only recommending use in severe cases, while most United States guidelines recommend medications in nearly all cases.

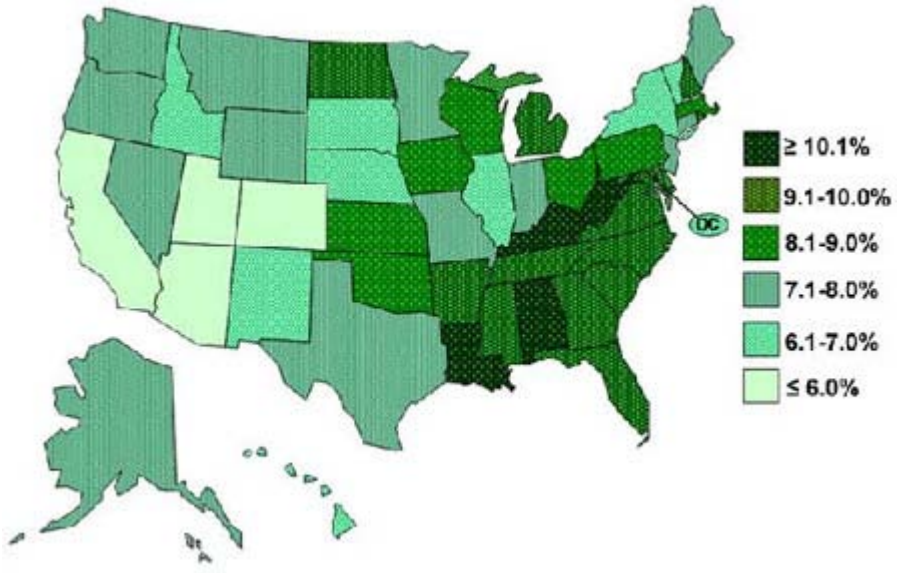
## *Prognosis*

Children diagnosed with ADHD have significant difficulties in adolescence, regardless of treatment. In the United States, 37 percent of those with ADHD do not get a high school diploma even though many of them will receive special education services. A 1995 briefing citing a 1994 book review says the combined outcomes of the expulsion and dropout rates indicate that almost half of all ADHD students never finish high school. Also in the US, less than 5 percent of individuals with ADHD get a college degree compared to 28 percent of the general population. Those with ADHD as children are at increased risk of a number of adverse life outcomes once they become teenagers. These include a greater risk of auto crashes, injury and higher medical expenses, earlier sexual activity, and teen pregnancy. Russell Barkley states that adult ADHD impairments affect "education, occupation, social relationships, sexual activities, dating and marriage, parenting and offspring psychological morbidity, crime and drug abuse, health and related lifestyles, financial management, or driving. ADHD can be found to produce diverse and serious impairments". The proportion of children meeting the diagnostic criteria for ADHD drops by about 50 percent over three years after the diagnosis. This occurs regardless of the treatments used and also occurs in untreated children with ADHD. ADHD persists into adulthood in about 30 to 50 percent of cases. Those affected are likely to develop coping mechanisms as they mature, thus compensating for their previous ADHD.

## *Epidemiology*




Percent of United States youth 4-17 ever diagnosed with ADHD as of 2007




Percent of United States youth 4-17 ever diagnosed with ADHD as of 2003

ADHD's global prevalence is estimated at 3 to 5 percent in people under the age of 19. There is, however, both geographical and local variability among studies. Geographically, children in North America appear to have a higher rate of ADHD than children in Africa and the Middle East, well published studies have found rates of ADHD as low as 2 percent and as high as 14 percent among school aged children. The rates of diagnosis and treatment of ADHD are also much higher on the East Coast of the USA than on the West Coast. The frequency of the diagnosis differs between male children (10%) and female children (4%) in the United States. This difference between genders

may reflect either a difference in susceptibility or that females with ADHD are less likely to be diagnosed than males.

Rates of ADHD diagnosis and treatment have increased in both the UK and the USA since the 1970s. In the UK an estimated 0.5 per 1,000 children had ADHD in the 1970s, while 3 per 1,000 received ADHD medications in the late 1990s. In the USA in the 1970s 12 per 1,000 children had the diagnosis, while in the late 1990s 34 per 1,000 had the diagnosis and the numbers continue to increase.

In the UK in 2003 a prevalence of 3.6 percent is reported in male children and less than 1 percent is reported in female children.

## *History*

Hyperactivity has long been part of the human condition. Sir Alexander Crichton describes "mental restlessness" in his book *An Inquiry Into the Nature and Origin of Mental Derangement* written in 1798. The terminology used to describe the symptoms of ADHD has gone through many changes over history including: "minimal brain damage", "minimal brain dysfunction" (or disorder), "learning/behavioral disabilities" and "hyperactivity". In the DSM-II (1968) it was the "Hyperkinetic Reaction of Childhood". In the DSM-III "ADD (Attention-Deficit Disorder) with or without hyperactivity" was introduced. In 1987 this was changed to ADHD in the DSM-III-R and subsequent editions. The use of stimulants to treat ADHD was first described in 1937.

## Legal status of medications

Stimulants legal status was recently reviewed by several international organizations:

- Internationally, methylphenidate is a Schedule II drug under the Convention on Psychotropic Substances.
- In the United States, methylphenidate is classified as a Schedule II controlled substance, the designation used for substances that have a recognized medical value but present a high likelihood for abuse because of their addictive potential.
- In the United Kingdom, methylphenidate is a controlled 'Class B' substance, and possession without prescription is illegal, with a sentence up to 14 years and/or an unlimited fine.
- In New Zealand, it is a 'class B2 controlled substance'. unlawful possession is punishable by 6 month prison sentence and distribution of it is punishable by a 14 year sentence.

## Controversies

ADHD and its diagnosis and treatment have been considered controversial since the 1970s. The controversies have involved clinicians, teachers, policymakers, parents and the media. Opinions regarding ADHD range from not believing it exists at all to believing there are genetic and physiological bases for the condition as well as

disagreement about the use of stimulant medications in treatment. Some sociologists consider ADHD to be a "classic example of the medicalization of deviant behavior, defining a previously nonmedical problem as a medical one". Most healthcare providers in U.S. accept that ADHD is a genuine disorder with debate in centering mainly around how it is diagnosed and treated. However,The British Psychological Society said in a 1997 report that physicians and psychiatrists should not follow the American example of applying medical labels to such a wide variety of attention-related disorders: "The idea that children who don't attend or who don't sit still in school have a mental disorder is not entertained by most British clinicians." In 2009, the British Psychological Society, in collaboration with the Royal College of Psychiatrists, released a set of guidelines for the diagnosis and treatment of ADHD. In its guideline, it state that available evidence indicate that ADHD is a valid diagnosis. However, it states that the diagnosis lack any biological basis and that "[c]ontroversial issues surround changing thresholds applied to the definition of illness as new knowledge and treatments are developed and the extent to which it is acknowledged that clinical thresholds are socially and culturally influenced and determine how an individual's level of dunctioning within the "normal cultural environment" is assessed. It further state that "the acceptable thresholds for impairment are partly driven by the contemporary societal view of what is an acceptable level of deviation from the norm."

Others have included that it may stem from a misunderstanding of the diagnostic criteria and how they are utilized by clinicians,[:p.3] teachers, policymakers, parents and the media. Debates center around: whether ADHD is a disability or whether it is merely a neurological description, the cause of the disorder, the changing of the diagnostic criteria, and the rapid increase in diagnosis of ADHD and the use of stimulants to treat the disorder. Long term possible side effects of stimulants and their usefulness are largely unknown because of a lack of long term studies. Some research raises questions about the long term effectiveness and side effects of medications used to treat ADHD.

In 1998, the US National Institutes of Health (NIH) released a consensus statement on the diagnosis and treatment of ADHD. The statement, while recognizing that stimulant treatment is controversial, supports the validity of the ADHD diagnosis and the efficacy of stimulant treatment. It found controversy only in the lack of sufficient data on long-term use of medications, and in the need for more research in many areas.

With a "wide variation in diagnosis across states, races, and ethnicities" some investigators suspect that factors other than neurological conditions play a role when the diagnosis of ADHD is made. Two studies published in 2010 suggest that the diagnosis is more likely to be made in the younger children within a grade; the authors propose that such a misdiagnosis of ADHD within a grade may be due to different states of maturity and may lead to potentially inappropriate treatment.

### *In adult*

Researchers found that 60 percent of the children diagnosed with ADHD continue having symptoms well into adulthood. Many adults, however, remain untreated. Untreated adults

with ADHD often have chaotic lifestyles, may appear to be disorganized and may rely on non-prescribed drugs and alcohol to get by. They often have such associated psychiatric comorbidities as depression, anxiety disorder, bipolar disorder, substance abuse, or a learning disability. A diagnosis of ADHD may offer adults insight into their behaviors and allow patients to become more aware and seek help with coping and treatment strategies. There is controversy amongst some experts on whether ADHD persists into adulthood. Recognized as occurring in adults in 1978, it is currently not addressed separately from ADHD in childhood. Obstacles that clinicians face when assessing adults who may have ADHD include developmentally inappropriate diagnostic criteria, age-related changes, comorbidities and the possibility that high intelligence or situational factors can mask ADHD.

# Chapter 13

# ADHD Predominantly Inattentive

**ADHD predominantly inattentive** (**ADHD-PI** or **ADHD-I**) is one of the three subtypes of Attention-deficit hyperactivity disorder (ADHD). While ADHD-PI is sometimes still called "**attention deficit disorder**" (**ADD**) by the general public, these older terms were formally changed in 1994 in the new Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV).

## *Differences from other ADHD subtypes*

ADHD-PI is different from the other subtypes of ADHD in that it is characterized primarily by inattention, easy distractibility, disorganization, procrastination, forgetfulness, and lethargy - fatigue, but with less or none of the symptoms of hyperactivity or impulsiveness typical of the other ADHD subtypes. In some cases, children who enjoy learning may develop a sense of fear when faced with structured or planned work, especially long or group-based that requires extended focus, even if they thoroughly understand the topic. Children with ADHD-PI may be at greater risk of academic failures and early withdrawal from school. Teachers and parents may make incorrect assumptions about the behaviours and attitudes of a child with undiagnosed ADHD-PI, and may provide them with frequent and erroneous negative feedback (e.g. "you're irresponsible", "you're immature", "you're lazy", "you don't care/show any effort", "you just aren't trying", etc.).

The inattentive children may realize on some level that they are somehow different internally from their peers. However, they are also likely to accept and internalize the continuous negative feedback, creating a negative self-image that becomes self-reinforcing. If these children progress into adulthood undiagnosed or untreated, their inattentiveness, ongoing frustrations, and poor self-image frequently create numerous and severe problems maintaining healthy relationships, succeeding in postsecondary schooling, or succeeding in the workplace. These problems can compound frustrations and low self-esteem, and will often lead to the development of secondary pathologies including anxiety disorders, mood disorders, and substance abuse.

It has been suggested by Patricia Quinn, among others, that some of the symptoms of ADHD present in childhood appear to be less overt in adulthood. This is likely due to an adult's ability to make cognitive adjustments and develop coping skills minimizing the frequency of inattentive or hyperactive behaviors. However, the core problems of ADHD

do not disappear with age. Some researchers have suggested that individuals with reduced or less overt hyperactivity symptoms should receive the ADHD-combined diagnosis. Hallowell and Ratey (2005) suggest that the manifestation of hyperactivity simply changes with adolescence and adulthood, becoming a more generalized restlessness or tendency to fidget.

In the DSM-III, sluggishness, drowsiness, and daydreaming were listed as characteristics of ADHD. The symptoms were removed from the ADHD criteria in DSM-IV because, although those with ADHD-PI were found to have these symptoms, this only occurred with the absence of hyperactive symptoms. These distinct symptoms were described as sluggish cognitive tempo (SCT).

A meta-analysis of 37 studies on cognitive differences between those with ADHD-Inattentive type and ADHD-Combined type found that "the ADHD/C subtype performed better than the ADHD/I subtype in the areas of processing speed, attention, performance IQ, memory, and fluency. The ADHD/I subtype performed better than the ADHD/C group on measures of flexibility, working memory, visual/spatial ability, motor ability, and language. Both the ADHD/C and ADHD/I groups were found to perform more poorly than the control group on measures of inhibition, however, there was no difference found between the two groups. Furthermore the ADHD/C and ADHD/I subtypes did not differ on measures of sustained attention."

Some experts, such as Dr. Russell Barkley, argue that ADHD-PI is so different from the other ADHD subtypes that it should be regarded as a distinct disorder. ADHD-PI is noted for the almost complete lack of conduct disorders and high-risk, thrill-seeking behavior. Further research needs to be done to discover differences among those with attention disorders.

## *Symptoms*

### DSM-IV criteria

The DSM-IV allows for diagnosis of the *predominantly inattentive* subtype of ADHD (under code 314.00) if the individual presents six or more of the following symptoms of inattention for at least six months to a point that is disruptive and inappropriate for developmental level:

- Often does not give close attention to details or makes careless mistakes in schoolwork, work, or other activities.
- Often has trouble keeping attention on tasks or play activities.
- Often does not seem to listen when spoken to directly.
- Often does not follow instructions and fails to finish schoolwork, chores, or duties in the workplace (not due to oppositional behavior or failure to understand instructions).
- Often has trouble organizing activities.

- Often avoids, dislikes, or doesn't want to do things that take a lot of mental effort for a long period (such as schoolwork or homework).
- Often loses things needed for tasks and activities (e.g. toys, school assignments, pencils, books, or tools).
- Is often easily distracted.
- Is often forgetful in daily activities.

A requirement for an ADHD-PI diagnosis is that of the symptoms that cause impairment must be present in two or more settings (e.g., at school or work and at home). There must also be clear evidence of clinically significant impairment in social, academic, or occupational functioning. Lastly, the symptoms must not occur exclusively during the course of a pervasive developmental disorder, schizophrenia, or other psychotic disorder, and are not better accounted for by another mental disorder (e.g., mood disorder, anxiety disorder, dissociative disorder, personality disorder).

Examples of observed symptoms

| Life Period | Example |
|---|---|
| Children | Failing to pay close attention to details or making careless mistakes when doing school-work or other activities |
| | Trouble keeping attention focused during play or tasks |
| | Appearing not to listen when spoken to (often being accused of "daydreaming") |
| | Failing to follow instructions or finish tasks |
| | Avoiding tasks that require a high amount of mental effort and organization, such as school projects |
| | Frequently losing items required to facilitate tasks or activities, such as school supplies |
| | Excessive distractibility |
| | Forgetfulness |
| | Procrastination, inability to begin an activity |
| | Difficulties completing household chores |
| Adults | Often making careless mistakes when having to work on uninteresting or difficult projects |
| | Often having difficulty keeping attention during work, or holding down a job for a significant amount of time |
| | Often having difficulty concentrating on conversations |
| | Having trouble finishing projects that have already been started |
| | Often having difficulty organizing for the completion of tasks |
| | Avoiding or delaying in starting projects that require a lot of thought |
| | Often misplacing or having difficulty finding things at home or at work |

Disorganized personal items (sometimes old and useless to the individual) causing excessive "clutter" (in the home, car, etc.)

Often distracted by activity or noise

Often having problems remembering appointments or obligations, or inconveniently changing plans on a regular basis

## *Prevalence*

It is difficult to say exactly how many children worldwide have ADHD because different countries have used different ways of diagnosing it, while some do not diagnose it at all. In the UK, diagnosis is based on quite a narrow set of symptoms, and about 0.5 - 1% of children are thought to have attention or hyperactivity problems. In comparison, until recently, professionals in the USA used a much broader definition of the term ADHD.

As a result, up to 10% of children in the USA were described as having ADHD. Current estimates suggest that ADHD is present throughout the world in about 1-5% of the population. About five times more boys than girls are diagnosed with ADHD. This may be partly because of the particular ways they express their difficulties. Boys and girls both have attention problems, but boys are more likely to be overactive and difficult to manage. Children from all cultures and social groups are diagnosed with ADHD. However, children from certain backgrounds may be particularly likely to be diagnosed with ADHD, because of different expectations about how they should behave. If you are a parent, it is therefore important to ensure that your child's cultural background is understood and taken into account as part of the assessment.

## *Treatment*

Recent studies indicate that medications approved by the U.S. Food and Drug Administration (FDA) in the treatment of ADHD tend to work well in individuals with the predominantly inattentive type. These medications include two classes of drugs, stimulants and non-stimulants. Drugs for ADHD are divided into first-line medications and second-line medications. First-line medications include several of the stimulants, and tend to have a higher response rate and effect size than second-line medications. Some of the most common stimulants are Methylphenidate (Ritalin), Adderall and Vyvanse.

Although medication can help improve concentration, it does not cure ADHD-I and the symptoms will come back once the medication stops. Moreover, medication works better for some patients while it barely works for others.

Also, along with medication, behavioral therapy is recommended to improve organizational skills, study techniques or social functioning.

There has been anecdotal evidence that dietary changes such as reducing food additives, colorings and sugars may be a useful treatment, however, there is no evidence from trials to support this information.

## *Research*

A recently funded study at the Mount Sinai AD/HD Center, supported by grants from the National Institutes of Health (NIH) will examine the use of functional Magnetic Resonance Imaging in identifying unique patterns of brain activation in children with ADHD-PI.

## *Strategies*

Parents are recommended to learn about this disorder in order to first be able to help themselves and then their children.

Behavioral strategies are of great help and they include creating routines, getting organized, avoiding distractions (television, video and computer games especially on weekdays during homework), limiting choices, using goals and rewards, ignoring behaviors.

Since children with ADHD can be extremely disorganized, parents should work with children to find specific places for everything and teach kids to use calendars and schedules. Parents are also advised to get children into sports to help them build discipline, confidence, and improve their social skills. Physical activity boosts the brain's dopamine, norepinephrine, and serotonin levels and all these substances affect focus and attention. However, some sports may be too challenging and would add frustration. Parents should talk to their children about what kinds of sports or exercise most stimulate and satisfy them before signing them up for classes or enrolling them in a given team sport.

It is very important to establish close communication with the school in order to develop an educational plan to address the child's needs. Accommodations in school such as extended time for tests or more frequent feedback from teachers are also beneficial for these individuals.

# Chapter 14

# Borderline Personality Disorder

## Borderline personality disorder

| | |
|---|---|
| **ICD-10** | (F60.3) |
| **ICD-9** | 301.83 |
| **MeSH** | D001883 |

**Borderline personality disorder** (**BPD**) is a personality disorder described as a prolonged disturbance of personality function in a person (generally over the age of eighteen years, although it is also found in adolescents), characterized by depth and variability of moods. The disorder typically involves unusual levels of instability in mood; black and white thinking, or splitting; the disorder often manifests itself in idealization and devaluation episodes, as well as chaotic and unstable interpersonal relationships, self-image, identity, and behavior; as well as a disturbance in the individual's sense of self. In extreme cases, this disturbance in the sense of self can lead to periods of dissociation.

BPD splitting includes a switch between idealizing and demonizing others. This, combined with mood disturbances, can undermine relationships with family, friends, and co-workers. BPD disturbances also may include self-harm. Without treatment, symptoms may worsen, leading (in extreme cases) to suicide attempts.

There is an ongoing debate among clinicians and patients worldwide about terminology and the use of the word *borderline*, and some have suggested that this disorder should be renamed. The ICD-10 manual has an alternative definition and terminology to this disorder, called *Emotionally unstable personality disorder*.

There is related concern that the diagnosis of BPD stigmatizes people and supports pejorative and discriminatory practices. It is common for those suffering from borderline personality disorder and their families to feel compounded by a lack of clear diagnoses, effective treatments, and accurate information. This is true especially because of evidence that this disorder originates in the families of those who suffer from it and has a lot to do with Axis IV factors, rather than belonging strictly in Axis II. Conceptual, as well as therapeutic, relief may be obtained through evidence that BPD is closely related to

traumatic events during childhood and to post-traumatic stress disorder (PTSD), about which much more is known.

## *Signs and symptoms*

Borderline personality disorder is a diagnosis about which many articles and books have been written, yet about which very little is known based on empirical research.

Studies suggest that individuals with BPD tend to experience frequent, strong and long-lasting states of aversive tension, often triggered by perceived rejection, being alone or perceived failure. Individuals with BPD may show lability (changeability) between anger and anxiety or between depression and anxiety and temperamental sensitivity to emotive stimuli.

The negative emotional states specific to BPD may be grouped into four categories: destructive or self-destructive feelings; extreme feelings in general; feelings of fragmentation or lack of identity; and feelings of victimization.

Individuals with BPD can be very sensitive to the way others treat them, reacting strongly to perceived criticism or hurtfulness. Their feelings about others often shift from positive to negative, generally after a disappointment or perceived threat of losing someone. Self-image can also change rapidly from extremely positive to extremely negative. Impulsive behaviors are common, including alcohol or drug abuse, unsafe sex, gambling and recklessness in general. Attachment studies suggest individuals with BPD, while being high in intimacy- or novelty-seeking, can be hyper-alert to signs of rejection or not being valued and tend toward insecure, avoidant or ambivalent, or fearfully preoccupied patterns in relationships. They tend to view the world generally as dangerous and malevolent, and tend to view themselves as powerless, vulnerable, unacceptable and unsure in self-identity.

Individuals with BPD are often described, including by some mental health professionals (and in the DSM-IV), as deliberately manipulative or difficult, but analysis and findings generally trace behaviors to inner pain and turmoil, powerlessness and defensive reactions, or limited coping and communication skills. There has been limited research on family members' understanding of borderline personality disorder and the extent of burden or negative emotion experienced or expressed by family members. However the effect of expressed emotion by family members may actually be opposite (paradoxical) from the anticipated effect on individuals with such illnesses as depressive disorders and schizophrenia. For BPD such effect may be neutral or positive as opposed to negative, a counter-intuitive result.

Parents of individuals with BPD have been reported to show co-existing extremes of over-involvement and under-involvement. BPD has been linked to increased levels of chronic stress and conflict in romantic relationships, decreased satisfaction of romantic partners, abuse and unwanted pregnancy; these links may be general to personality disorder and subsyndromal problems.

Suicidal or self-harming behavior is one of the core diagnostic criteria in DSM IV-TR, and management of and recovery from this can be complex and challenging. The suicide rate is approximately 8 to 10 percent. Self-injury attempts are highly common among patients and may or may not be carried out with suicidal intent. BPD is often characterized by multiple low-lethality suicide attempts triggered by seemingly minor incidents, and less commonly by high-lethality attempts that are attributed to impulsiveness or comorbid major depression, with interpersonal stressors appearing to be particularly common triggers. Ongoing family interactions and associated vulnerabilities can lead to self-destructive behavior. Stressful life events related to sexual abuse have been found to be a particular trigger for suicide attempts by adolescents with a BPD diagnosis.

## *Diagnosis*

Diagnosis is based on a clinical assessment by a qualified mental health professional. The assessment incorporates the patient's self-reported experiences as well as the clinician's observations. The resulting profile may be supported or corroborated by long-term patterns of behavior as reported by family members, friends or co-workers. The list of criteria that must be met for diagnosis is outlined in the DSM-IV-TR.

Borderline personality disorder was once classified as a subset of schizophrenia (describing patients with borderline schizophrenic tendencies). Today BPD is used more generally to describe individuals who display emotional dysregulation and instability, with paranoid schizophrenic ideation or delusions being only one criterion (criterion #9) of a total of 9 criteria, of which 5, or more, must be present for this diagnosis.

Individuals with BPD are at high risk of developing other psychological disorders such as anxiety and depression. Other symptoms of BPD, such as dissociation, are frequently linked to severely traumatic childhood experiences, which some put forth as one of the many root causes of the borderline personality.

### Adolescence

Onset of symptoms typically occurs during adolescence or young adulthood. Symptoms may persist for several years, but the majority of symptoms lessen in severity over time, with some individuals fully recovering. The mainstay of treatment is various forms of psychotherapy, although medication and other approaches may also improve symptoms. While borderline personality disorder can manifest itself in children and teenagers, therapists are discouraged from diagnosing anyone before the age of 18, due to adolescence and a still-developing personality.

There are some instances when BPD can be evident and diagnosed before the age of 18. The DSM-IV states: "To diagnose a personality disorder in an individual under 18 years, the features must have been present for at least 1 year." In other words, it is possible to diagnose the disorder in children and adolescents, but a more conservative approach should be taken.

There is some evidence that BPD diagnosed in adolescence is predictive of the disease continuing into adulthood. It is possible that the diagnosis, if applicable, would be helpful in creating a more effective treatment plan for the child or teen.

## Diagnostic and Statistical Manual

The Diagnostic and Statistical Manual of Mental Disorders fourth edition, DSM IV-TR, a widely used manual for diagnosing mental disorders, defines borderline personality disorder (in Axis II Cluster B) as:

> A pervasive pattern of instability of interpersonal relationships, self-image and affects, as well as marked impulsivity, beginning by early adulthood and present in a variety of contexts, as indicated by five (or more) of the following:
>
> 1. Frantic efforts to avoid real or imagined abandonment. **Note:** Do not include suicidal or self-injuring behavior covered in Criterion 5
> 2. A pattern of unstable and intense interpersonal relationships characterized by alternating between extremes of idealization and devaluation.
> 3. Identity disturbance: markedly and persistently unstable self-image or sense of self.
> 4. Impulsivity in at least two areas that are potentially self-damaging (e.g., promiscuous sex, eating disorders, binge eating, substance abuse, reckless driving). **Note:** Do not include suicidal or self-injuring behavior covered in Criterion 5
> 5. Recurrent suicidal behavior, gestures, threats or self-injuring behavior such as cutting, interfering with the healing of scars (excoriation) or picking at oneself.
> 6. Affective instability due to a marked reactivity of mood (e.g., intense episodic dysphoria, irritability or anxiety usually lasting a few hours and only rarely more than a few days).
> 7. Chronic feelings of emptiness
> 8. Inappropriate anger or difficulty controlling anger (e.g., frequent displays of temper, constant anger, recurrent physical fights).
> 9. Transient, stress-related paranoid ideation, delusions or severe dissociative symptoms

It is a requirement of DSM-IV that a diagnosis of any specific personality disorder also satisfies a set of general personality disorder criteria.

## International Classification of Disease

The World Health Organization's ICD-10 defines a conceptually similar disorder to borderline personality disorder called *(F60.3) Emotionally unstable personality disorder*. It has two subtypes described below.

F60.30 Impulsive type

At least three of the following must be present, one of which must be (2):

1. marked tendency to act unexpectedly and without consideration of the consequences;
2. marked tendency to quarrelsome behaviour and to conflicts with others, especially when impulsive acts are thwarted or criticized;
3. liability to outbursts of anger or violence, with inability to control the resulting behavioural explosions;
4. difficulty in maintaining any course of action that offers no immediate reward;
5. unstable and capricious mood.

It is a requirement of ICD-10 that a diagnosis of any specific personality disorder also satisfies a set of general personality disorder criteria.

F60.31 Borderline type

At least three of the symptoms mentioned in *F60.30 Impulsive type* must be present, with at least two of the following in addition:

1. disturbances in and uncertainty about self-image, aims, and internal preferences (including sexual);
2. liability to become involved in intense and unstable relationships, often leading to emotional crisis;
3. excessive efforts to avoid abandonment;
4. recurrent threats or acts of self-harm;
5. chronic feelings of emptiness.

It is a requirement of ICD-10 that a diagnosis of any specific personality disorder also satisfies a set of general personality disorder criteria.

## Chinese Society of Psychiatry

The Chinese Society of Psychiatry's CCMD has a comparable diagnosis of Impulsive Personality Disorder (IPD). A patient diagnosed as having IPD must display "affective outbursts" and "marked impulsive behavior," plus at least three out of eight other symptoms. The construct has been described as a hybrid of the impulsive and borderline subtypes of the ICD-10's Emotionally Unstable Personality Disorder, and also incorporates six of the nine DSM BPD criteria.

## Millon's subtypes

Theodore Millon identified four subtypes of borderline. Any individual borderline may exhibit none, or one or more of the following:

- Discouraged borderline — including avoidant, depressive or dependent features
- Impulsive borderline — including histrionic or antisocial features

- Petulant borderline — including negativistic (passive-aggressive) features
- Self-destructive borderline — including depressive or masochistic features

## Differential diagnosis

Common comorbid (co-occurring) conditions are mental disorders such as substance abuse, depression and other mood and personality disorders.

Borderline personality disorder and mood disorders often appear concurrently. Some features of borderline personality disorder may overlap with those of mood disorders, complicating the differential diagnostic assessment.

Both diagnoses involve symptoms commonly known as "mood swings." In borderline personality disorder, the term refers to the marked lability and reactivity of mood defined as emotional dysregulation. The behavior is typically in response to external psychosocial and intrapsychic stressors, and may arise or subside, or both, suddenly and dramatically and last for seconds, minutes, hours, days, weeks or months.

Bipolar depression is generally more pervasive with sleep and appetite disturbances, as well as a marked nonreactivity of mood, whereas mood with respect to borderline personality and co-occurring dysthymia remains markedly reactive and sleep disturbance not acute.

The relationship between bipolar disorder and borderline personality disorder has been debated. Some hold that the latter represents a subthreshold form of affective disorder, while others maintain the distinctness between the disorders, noting they often co-occur.

Some findings suggest that BPD may lie on a bipolar spectrum, with a number of points of phenomenological and biological overlap between the affective lability criterion of borderline personality disorder and the extremely rapid cycling bipolar disorders. Some findings suggest that the DSM-IV BPD diagnosis mixes up two sets of unrelated items—an affective instability dimension related to Bipolar-II, and an impulsivity dimension not related to Bipolar-II.

It is important to emphasize that medical conditions which cause organic behavioral function may result in a clinical picture that mimics to some degree BPD. Hormonal dysfunction over a long period, or brain dysfunction (e.g. the encephalopathy caused by lyme disease) can result in identity disturbance and mood lability, as can many other chronic medical conditions such as lupus. These conditions may isolate the patient socially and emotionally, and/or cause limbic damage to the brain. However, this is not borderline personality disorder which results, but rather a reaction to the isolating circumstances caused by a medical condition and the possibly coincident struggles of the patient to control his or her mood given damage to the brain's limbic system. Heavy alcohol usage over a long period itself can cause an encephalopathy which may cause limbic damage. Various frontal lobe syndromes can result in disinhibition and impulsive behavior.

Comorbid (co-occurring) conditions in BPD are common. When comparing individuals diagnosed with BPD to those diagnosed with other personality disorders, the former showed a higher rate of also meeting criteria for:

- Autism Spectrum Disorder (ASD)
- anxiety disorders
- mood disorders (including clinical depression and bipolar disorder)
- eating disorders (including anorexia nervosa and bulimia)
- and, to a lesser extent, somatoform or factitious disorders
- dissociative disorders
- Substance abuse is a common problem in BPD, whether due to impulsivity or as a coping mechanism, and 50 percent to 70 percent of psychiatric inpatients with BPD have been found to meet criteria for a substance use disorder, especially alcohol dependence or abuse which is often combined with the abuse of other drugs.

## *Causes*

As with other mental disorders, the causes of BPD are complex and not fully understood. One finding is a history of childhood trauma, abuse or neglect, although researchers have suggested diverse possible causes, such as a genetic predisposition, neurobiological factors, environmental factors, or brain abnormalities.

There is evidence that suggests that BPD and post-traumatic stress disorder (PTSD) are closely related. Evidence further suggests that BPD might result from a combination that can involve a traumatic childhood, a vulnerable temperament and stressful maturational events during adolescence or adulthood.

### Childhood abuse

Numerous studies have shown a strong correlation between child abuse, especially child sexual abuse, and development of BPD. Many individuals with BPD report to have had a history of abuse and neglect as young children. Patients with BPD have been found to be significantly more likely to report having been verbally, emotionally, physically or sexually abused by caregivers of either gender. There has also been a high incidence of incest and loss of caregivers in early childhood for people with borderline personality disorder. They were also much more likely to report having caregivers (of both genders) deny the validity of their thoughts and feelings. They were also reported to have failed to provide needed protection, and neglected their child's physical care. Parents (of both sexes) were typically reported to have withdrawn from the child emotionally, and to have treated the child inconsistently. Additionally, women with BPD who reported a previous history of neglect by a female caregiver and abuse by a male caregiver were consequently at significantly higher risk for being sexually abused by a noncaregiver (not a parent). It has been suggested that children who experience chronic early maltreatment and attachment difficulties may go on to develop borderline personality disorder.

## Other developmental factors

Some studies suggest that BPD may not necessarily be a trauma-spectrum disorder and that it is biologically distinct from the post-traumatic stress disorder that could be a precursor. The personality symptom clusters seem to be related to specific abuses, but they may be related to more persistent aspects of interpersonal and family environments in childhood.

Otto Kernberg formulated the theory of borderline personality based on a premise of failure to develop in childhood. Writing in the psychoanalytic tradition, Kernberg argued that failure to achieve the developmental task of *psychic clarification of self and other* can result in an increased risk to develop varieties of psychosis, while failure to *overcome splitting* results in an increased risk to develop a borderline personality.

## Genetics

An overview of the existing literature suggested that traits related to BPD are influenced by genes. A major twin study found that if one identical twin met criteria for BPD, the other also met criteria in 35 percent of cases. People that have BPD influenced by genes usually have a close relative with the disorder.

Twin, sibling and other family studies indicate a partially heritable basis for impulsive aggression, but studies of serotonin-related genes to date have suggested only modest contributions to behavior.

## Mediators and moderators

While research has examined variables that predict the development of borderline personality disorder (BPD), researchers have only recently begun to examine the variables that mediate and moderate the relationships between these variables and the development of the disorder. A mediator is a variable that affects how the relationship occurs. Mediation is said to be present when both the predictor variable and the mediating variable are significantly correlated with the dependent variable, and when the relationship between the predictor variable and the outcome variable is significantly reduced when controlling for the mediating variable. A moderating variable by contrast specifies the conditions under which a given outcome will occur. Moderation is said to occur when there is an interaction effect between the predicting variable and the moderating variable on the dependent variable. More specifically, the effect of the predicting variable is different depending on the level of the moderating variable.

Research has found statistically significant relationships between BPD symptoms and both sexual and physical abuse. Other factors including family environment variables also contribute to the development of the disorder. Bradley et al. found that both child sexual abuse (CSA) and childhood physical abuse and BPD symptoms were significantly related, and both CSA and childhood physical abuse were significantly related to family environment. When family environment and childhood physical abuse were entered

simultaneously into a regression equation, family environment was related to BPD symptoms and childhood physical abuse was related to BPD symptoms, although the relationship between BPD symptoms and childhood physical abuse was reduced. Therefore, CSA and childhood physical abuse both directly influence the development of BPD symptoms directly and are mediated by family environment.

Other research has examined the relationship between negative affectivity, thought suppression and BPD symptoms. The results of the mediational models in this study found that thought suppression mediated the relationship between negative affectivity and BPD symptoms. While negative affectivity significantly predicted BPD symptoms after controlling for CSA, this relationship was greatly reduced when thought suppression was introduced into the model. Thus, the relationship of negative affectivity to BPD symptoms is mediated by thought suppression.

Ayduk et al. (2008) found an interaction between rejection sensitivity and executive control in the prediction of BPD symptoms. This study found that BPD features were positively associated with rejection sensitivity (RS) and neuroticism and negatively associated with emotional control (EC). Their statistical analysis indicated that among those low in EC, RS was positively related to BPD features and among those high in RS, EC was negatively associated with BPD. By contrast, among those high in EC, RS was not significantly related to BP features, and among those low in RS, EC was not related to BPD features. In Study 2, BPD features were positively correlated to RS and negatively correlated with executive control. Additionally, the authors found that delay gratification times at age 4 had no significant relationship with BPD features at the time of the current study. Again, as in Study 1, the RS x EC interaction was significant. Among those low in EC, RS was positively related to BPD features, while among those high in EC, the effect of RS was reduced to marginal significance. Moreover, among those high in RS, EC was negatively associated with BPD features, but among those low in RS, EC was unrelated to BPD features.

Parker, Boldero and Bell (2006) indicated that both AI and AO self-discrepancy magnitudes were strongly correlated to each other and to BPD features. Self-complexity was not significantly related to any of the other factors. Among those high in self-complexity, the relationship between AI self-discrepancy magnitudes and BPD features was lower than among those with less self-complexity. Actual-ought self-discrepancy relationship with BPD features was not significantly moderated by self-complexity.

BPD is complex, and several factors have an impact on whether clinical features of BPD are present. None of the prediction factors above are sufficient to be the key factor in the development of BPD features. Increased knowledge of the development of the disorder may help prevent symptom aggravation and identify new treatment strategies. Future research should integrate the knowledge gained from these areas and study these variables simultaneously. Studies in which these variables are simultaneously examined would provide greater specificity in the relationships between the variables. These articles taken together not only increase our knowledge of what factors and variables lead

to the development of BPD features and BPD itself but also, when taken together, indicate future lines of research yet to be studied.

## *Management*

Treatment options for borderline personality disorder includs psychotherapeutic methods. Methods especially developt for the treatment of Borderline or other personalty disorders are: dialectical behavior therapy, transference focused psychotherapy and mentalization-based treatment. There are no specific medication for BPD however some symptoms may be managed with medication.

The UK's National Institute for Health and Clinical Excellence (NICE) states that BPD treatments be based on individual case presentation, rather than upon the diagnosis of BPD. NICE encourages doctors to use co-morbid conditions to determine which medications, if any, are appropriate. A Cochrane review from 2006 arrived at the same conclusion. Antidepressants, antipsychotics and mood stabilisers (such as lithium) are regularly used to treat co-morbid symptoms such as depression. Hospitalization has not been found to improve outcomes or prevent suicide over community care in those with BPD.

## Services and recovery

Individuals with BPD sometimes use mental health services extensively. People with this diagnosis accounted for about 20 percent of psychiatric hospitalizations in one survey. The majority of BPD patients continue to use outpatient treatment in a sustained manner for several years, but the number using the more restrictive and costly forms of treatment, such as inpatient admission, declines with time. Experience of services varies. Assessing suicide risk can be a challenge for mental health services (and patients themselves tend to underestimate the lethality of self-injurious behaviours) with typically a chronically elevated risk of suicide much above that of the general population and a history of multiple attempts when in crisis.

Particular difficulties have been observed in the relationship between care providers and individuals diagnosed with BPD. A majority of psychiatric staff report finding individuals with BPD moderately to extremely difficult to work with, and more difficult than other client groups. Some clients feel a diagnosis is helpful, allowing them to understand they are not alone, and to connect with others who have BPD and who have developed helpful coping mechanisms. On the other hand, some with the diagnosis of BPD have reported that the term "BPD" felt like a pejorative label rather than a helpful diagnosis, that self-destructive behaviour was incorrectly perceived as manipulative, and that they had limited access to care. Attempts are made to improve public and staff attitudes.

The American Psychiatric Association reports that recent advancements have led to treatments reaching an 86% remission rate 10 years after treatment.

## *Epidemiology*

The prevalence of BPD in the general population ranges from 1 to 2 percent. The diagnosis appears to be several times more common in (especially young) women than in men, by as much as 3:1, according to the DSM-IV-TR, although the reasons for this are not clear.

The prevalence of BPD in the United States has been calculated as 1 percent to 3 percent of the adult population, with approximately 75 percent of those diagnosed being female. It has been found to account for 20 percent of psychiatric hospitalizations.

## *History*

Since the earliest record of medical history, the coexistence of intense, divergent moods within an individual has been recognized by such writers as Homer, Hippocrates and Aretaeus, the last describing the vacillating presence of impulsive anger, melancholia and mania within a single person. After medieval suppression of the concept, it was revived by Swiss physician Théophile Bonet in 1684, who, using the term *folie maniaco-mélancolique*, noted the erratic and unstable moods with periodic highs and lows that rarely followed a regular course. His observations were followed by those of other writers who noted the same pattern, including writers such as the American psychiatrist C. Hughes in 1884 and J.C. Rosse in 1890, who described "borderline insanity". Kraepelin, in 1921, identified an "excitable personality" that closely parallels the borderline features outlined in the current concept of borderline.

Adolf Stern wrote the first significant psychoanalytic work to use the term "borderline" in 1938, referring to a group of patients with what was thought to be a mild form of schizophrenia, on the borderline between neurosis and psychosis. For the next decade the term was in popular and colloquial use, a loosely conceived designation mostly used by theorists of the psychoanalytic and biological schools of thought. Increasingly, theorists who focused on the operation of social forces were recognized as well.

The 1960s and 1970s saw a shift from thinking of the borderline syndrome as borderline *schizophrenia* to thinking of it as a borderline *affective disorder* (mood disorder), on the fringes of manic depression, cyclothymia and dysthymia. In DSM-II, stressing the affective components, it was called cyclothymic personality (affective personality). In parallel to this evolution of the term "borderline" to refer to a distinct category of disorder, psychoanalysts such as Otto Kernberg were using it to refer to a broad spectrum of issues, describing an intermediate level of personality organization between neurotic and psychotic processes.

Standardized criteria were developed to distinguish BPD from affective disorders and other Axis I disorders, and BPD became a personality disorder diagnosis in 1980 with the publication of DSM-III. The diagnosis was formulated predominantly in terms of mood and behavior, distinguished from sub-syndromal schizophrenia which was termed

"Schizotypal personality disorder". The final terminology in use by the DSM today was decided by the DSM-IV Axis II Work Group of the American Psychiatric Association.

## *Controversies*

### Gender

The diagnosis of BPD has been criticized from a feminist perspective. This is because some of the diagnostic criteria/symptoms of the disorder uphold common gender stereotypes about women. For example, the criteria of "a pattern of unstable personal relationships, unstable self-image, and instability of mood," can all be linked to the stereotype that women are "neither decisive nor constant". The question has also been raised of why women are three times more likely to be diagnosed with BPD than men. Some think that people with BPD commonly have a history of sexual abuse in childhood. One feminist critique suggests that BPD is a stigmatizing diagnosis that can sometimes evoke negative responses from health care providers, and additionally, that women who have survived sexual abuse in childhood are therefore sometimes re-traumatized by any such abusive mental health service.

Some feminist writers have suggested it would be better to give these women the diagnosis of a post-traumatic disorder as this would acknowledge their abuse, but others have argued that the use of the PTSD diagnosis merely medicalizes abuse rather than addressing the root causes in society. Women may be more likely to receive a personality disorder diagnosis if they reject the female role by being hostile, successful or sexually active; alternatively if a woman presents with psychiatric symptoms but does not conform to a traditional passive sick role, she may be labelled as a "difficult" patient and given the stigmatizing diagnosis of BPD.

### Stigma

The features of BPD include emotional instability, intense unstable interpersonal relationships, a need for relatedness and a fear of rejection. As a result, people with BPD often evoke intense emotions in those around them. Pejorative terms to describe persons with BPD such as “difficult,” “treatment resistant,” “manipulative,” “demanding” and “attention seeking" are often used, and may become a self-fulfilling prophecy as the clinician's negative response triggers further self-destructive behaviour. In psychoanalytic theory, this stigmatization may be thought to reflect countertransference (when a therapist projects their own feelings on to a client), as people with BPD are prone to use defense mechanisms such as splitting and projective identification. Thus the diagnosis "often says more about the clinician's negative reaction to the patient than it does about the patient ... as an expression of counter transference hate, borderline explains away the breakdown in empathy between the therapist and the patient and becomes an institutional epithet in the guise of pseudoscientific jargon" (Aronson, p 217).

This inadvertent counter transference can give rise to inappropriate clinical responses including excessive use of medication, inappropriate mothering and punitive use of limit

setting and interpretation. People with BPD are seen as among the most challenging groups of patients, requiring a high degree of skill and training in the psychiatrists, therapists and nurses involved in their treatment. While some clinicians agree with the diagnosis under the name "borderline personality disorder", some would like the name to be changed. One critique says that some who are labeled "Borderline Personality Disorder" feel this name is unhelpful, stigmatizing, and/or inaccurate.

The Treatment and Research Advancements National Association for Personality Disorders (TARA-APD) campaigns to change the name and designation of BPD in DSM-5. The paper *How Advocacy is Bringing BPD into the Light* reports that "the name BPD is confusing, imparts no relevant or descriptive information, and reinforces existing stigma."

## Terminology

Because of the above concerns, and because of a move away from the original theoretical basis for the term, there is ongoing debate about renaming BPD. Alternative suggestions for names include *emotional regulation disorder* or *emotional dysregulation disorder*. *Impulse disorder* and *interpersonal regulatory disorder* are other valid alternatives, according to John Gunderson of McLean Hospital in the United States. Another term (for example, by psychiatrist Carolyn Quadrio) is *post traumatic personality disorganization* (PTPD), reflecting the condition's status as (often) both a form of chronic post traumatic stress disorder (PTSD) and a personality disorder in the belief that it is a common outcome of developmental or attachment trauma. Some people do not report any kind of traumatic event.

# Chapter 15

# Obsessive–Compulsive Disorder

## Obsessive–compulsive disorder

Repetitive handwashing is a common OCD symptom

| | |
|---|---|
| **ICD-10** | F42. |
| **ICD-9** | 300.3 |
| **DiseasesDB** | 33766 |
| **MeSH** | D009771 |

**Obsessive–compulsive disorder** (**OCD**) is an anxiety disorder characterized by intrusive thoughts that produce uneasiness, apprehension, fear, or worry, by repetitive behaviors aimed at reducing anxiety, or by a combination of such thoughts (obsessions) and behaviors (compulsions). Symptoms may include repetitive handwashing; extensive hoarding; preoccupation with sexual or aggressive impulses, or with particular religious beliefs; aversion to odd numbers; and nervous habits, such as opening a door and closing it a certain number of times before one enters or leaves a room. These symptoms can be alienating and time-consuming, and often cause severe emotional and financial distress. The acts of those who have OCD may appear paranoid and come across to others as psychotic. However, OCD sufferers generally recognize their thoughts and subsequent actions as irrational, and they may become further distressed by this realization.

OCD is the fourth-most-common mental disorder, and is diagnosed nearly as often as asthma and diabetes mellitus. In the United States, one in 50 adults has OCD. Obsessive–compulsive disorder affects children and adolescents as well as adults. Roughly one third to one half of adults with OCD report a childhood onset of the disorder, suggesting the continuum of anxiety disorders across the life span. The phrase "obsessive–compulsive" has become part of the English lexicon, and is often used in an informal or caricatured manner to describe someone who is meticulous, perfectionistic, absorbed in a cause, or otherwise fixated on something or someone. Although these signs may be present in OCD, a person who exhibits them does not necessarily have OCD, and may instead have obsessive–compulsive *personality* disorder (OCPD), an autism spectrum disorder, or no clinical condition. Multiple psychological and biological factors may be involved in causing obsessive–compulsive syndromes.

Standardized rating scales such as Yale–Brown Obsessive Compulsive Scale can be used to assess severity of OCD symptoms.

## *Signs and symptoms*

### Obsessions

A typical person with OCD performs tasks, or compulsions, to seek relief from obsession-related anxiety. Within and among individuals, the initial obsessions, or intrusive thoughts, can vary in their clarity and vividness. A relatively vague obsession could involve a general sense of disarray or tension accompanied by a belief that life cannot proceed as normal while the imbalance remains. A more articulable obsession could be a preoccupation with the thought or image of someone close to them dying. Other obsessions concern the possibility that someone or something other than oneself—such as God, the Devil, or disease—will harm either the person with OCD or the people or things that the person cares about. Others may sense that the physical world is qualified by certain immaterial conditions. These people might intuit invisible protrusions from their bodies, or could feel that inanimate objects are ensouled.

Some people with OCD experience sexual obsessions that may involve intrusive thoughts or images of "kissing, touching, fondling, oral sex, anal sex, intercourse, incest and rape" with "strangers, acquaintances, parents, children, family members, friends, coworkers, animals and religious figures", and can include "heterosexual or homosexual content" with persons of any age. As with other intrusive, unpleasant thoughts or images, most people have some disquieting sexual thoughts at times, but people with OCD may attach extraordinary significance to the thoughts. For example, obsessive fears about sexual orientation can appear to the person with OCD, and even to those around them, as a crisis of sexual identity. Furthermore, the doubt that accompanies OCD leads to uncertainty regarding whether one might act on the troubling thoughts, resulting in self-criticism or self-loathing.

People with OCD understand that their notions do not correspond with the external world; however, they feel that they must act as though their notions were correct. For

example, an individual who engages in compulsive hoarding might be inclined to treat inorganic matter as if it had the sentience or rights of living organisms, but such an individual might find their consequent behavior irrational on a more intellectual level. In severe OCD, obsessions can shift into delusions when resistance to the obsession is abandoned and insight into its senselessness is lost. (Insel and Akiskal (1986))

## Compulsions

While some people with OCD perform compulsive rituals because they inexplicably feel they have to, others act compulsively so as to mitigate the anxiety that stems from particular obsessive thoughts. The person with OCD might feel that these actions somehow either will prevent a dreaded event from occurring, or will push the event from their thoughts. In any case, the individual's reasoning is so idiosyncratic or distorted that it results in significant distress for the individual with OCD or for those around them. Excessive skin picking (i.e., dermatillomania) or hair plucking (i.e., trichotillomania) and nail biting (i.e., onychophagia) are all on the Obsessive-Compulsive Spectrum. Individuals with OCD are aware that their thoughts and behavior are not rational, but they feel bound to comply with them to fend off feelings of panic or dread.

Some common compulsions include counting specific things (such as footsteps) or in specific ways (for instance, by intervals of two) and doing other repetitive actions, often with atypical sensitivity to numbers or patterns. People might repeatedly wash their hands or clear their throats, making sure certain items are in a straight line, repeatedly check that their parked cars have been locked before leaving them, constantly organizing in a certain way, turn lights on and off, keep doors closed at all times, touch objects a certain number of times before exiting a room, walk in a certain routine way like only stepping on a certain color of tile, or have a routine for using stairs, such as always finishing a flight on the same foot.

People rely on compulsions as an escape from their obsessive thoughts; however, they are aware that the relief is only temporary, that the intrusive thoughts will soon come back. Some people use compulsions to avoid situations that may trigger their obsessions. Although some people do certain things over and over again, they don't necessarily perform these actions compulsively. For example, bedtime routines, learning a new skill, and religious practices are not compulsions. Whether or not behaviors are compulsions or mere habit depends on the context in which the behaviors are performed. For example, arranging and ordering DVDs for eight hours a day would be expected of one who works in a video store, but would seem abnormal in other situations. In other words, habits tend to bring efficiency to one's life, while compulsions tend to interfere with it.

In addition to the anxiety and fear that typically accompanies OCD, some people may spend hours performing such tasks (i.e., compulsions) every day. In such situations it can be hard for the person to fulfill their work, family, or social roles. In some cases, these behaviors can also cause adverse physical symptoms. For example, people who obsessively wash their hands with antibacterial soap and hot water to remove what they consider to be contamination can make their skin red and raw with dermatitis.

People with OCD can use rationalizations to explain their behavior; however these rationalizations do not apply to the overall behavior but to each instance individually; for example, a person compulsively checking the front door may argue that the time taken and stress caused by one more check of the front door is much less than the time and stress associated with being robbed, and thus the check is the better option. In practice, after that check, the person is *still* not sure and deems it is *still* better in terms of time and stress to do one more check, and this reasoning can continue as long as necessary.

### OCD without overt compulsions

OCD sometimes manifests without overt compulsions. Nicknamed "Pure-O", OCD without overt compulsions could, by one estimate, characterize as many as 50 percent to 60 percent of OCD cases. Rather than engaging in observable compulsions, the person with this subtype might perform more covert, mental rituals, or might feel driven to avoid the situations in which particular thoughts seem likely to intrude. As a result of this avoidance, people can struggle to fulfill both public and private roles, even if they place great value on these roles and even if they had fulfilled the roles successfully in the past. Moreover, the individual's avoidance can confuse others who do not know its origin or intended purpose, as it did in the case of a man whose wife began to wonder why he would not hold their infant child.

## *Etiology*

Scholars generally agree that both psychological and biological factors play a role in causing the disorder, although they differ in their degree of emphasis upon either type of factor.

### Psychological

Obsessive–compulsive disorder (OCD) is a psychiatric anxiety disorder that includes distressing, intrusive thoughts and related compulsions (tasks or "rituals") to neutralize the obsessions. Obsessions are usually upsetting and the compulsions lead to temporary feelings of relief. To be diagnosed with obsessive-compulsive disorder, one must have either obsessions or compulsions alone, or obsessions and compulsions together, but most people with OCD have both.

Obsessions are:

- Recurrent and persistent thoughts, impulses, or images that are intrusive and inappropriate. The thoughts cause severe anxiety or distress.
- The thoughts, impulses, or images are not just excessive worries about real-life problems.
- The person tries to ignore or suppress the thoughts, impulses, or images, or to neutralize them with some other thought or action.
- The person recognizes that the obsessional thoughts, impulses, or images are a product of his or her own mind, and are not based in reality.

Compulsions are:

- Repetitive behaviors or mental acts that the person feels they must perform in response to an obsession, or according to rigid rules.
- The behaviors or mental acts to prevent or reduce distress or prevent some dreaded event or situation; however, these behaviors or mental acts either are not connected in a realistic way with what they are supposed to neutralize or prevent or are clearly excessive.

In addition, at some point during the course of the disorder, the person must realize that his/her obsessions or compulsions are unreasonable or excessive, which is why people with OCD are not considered to be detached from reality or psychotic. The obsessions or compulsions must be time-consuming, taking up more than one hour per day, cause distress, or cause difficulty in social, work, or school functioning. Having OCD is stressful and can lead to feelings of hopelessness and depression.

## Biological

OCD has been linked to abnormalities with the neurotransmitter serotonin, although it could be either a cause or an effect of these abnormalities. Serotonin is thought to have a role in regulating anxiety. To send chemical messages from one neuron to another, serotonin must bind to the receptor sites located on the neighboring nerve cell. It is hypothesized that the serotonin receptors of OCD sufferers may be relatively understimulated. This suggestion is consistent with the observation that many OCD patients benefit from the use of selective serotonin reuptake inhibitors (SSRIs), a class of antidepressant medications that allow for more serotonin to be readily available to other nerve cells.

A possible genetic mutation may contribute to OCD. A mutation has been found in the human serotonin transporter gene, hSERT, in unrelated families with OCD. Moreover, data from identical twins supports the existence of a "heritable factor for neurotic anxiety". Further, individuals with OCD are more likely to have first-degree family members exhibiting the same disorders than do matched controls. In cases where OCD develops during childhood, there is a much stronger familial link in the disorder than cases in which OCD develops later in adulthood. In general, genetic factors account for 45-65% of OCD symptoms in children diagnosed with the disorder. Environmental factors also play a role in how these anxiety symptoms are expressed; various studies on this topic are in progress and the presence of a genetic link is not yet definitely established.

People with OCD evince increased grey matter volumes in bilateral lenticular nuclei, extending to the caudate nuclei, while decreased grey matter volumes in bilateral dorsal medial frontal/anterior cingulate gyri. These findings contrast with those in people with other anxiety disorders, who evince decreased (rather than increased) grey matter volumes in bilateral lenticular / caudate nuclei, while also decreased grey matter volumes in bilateral dorsal medial frontal/anterior cingulate gyri. OFC overactivity is attenuated in

patients who have successfully responded to SSRI medication, a result believed to be caused by increased stimulation of serotonin receptors 5-HT2A and 5-HT2C. The striatum, linked to planning and the initiation of appropriate actions, has also been implicated; mice genetically engineered with a striatal abnormality exhibit OCD-like behavior, grooming themselves three times as frequently as ordinary mice. Recent evidence supports the possibility of a heritable predisposition for neurological development favoring OCD.

Rapid onset of OCD in children may be caused by Group A streptococcal infection, a condition hypothesized by its acronym PANDAS.

### Neurotransmitters role

Researchers have yet to pinpoint the exact cause of obsessive-compulsive disorder (OCD), but brain differences, genetic influences, and environmental factors are being studied. Brain scans of people with OCD have shown that they have different patterns of brain activity than people without OCD and that different functioning of circuitry within a certain part of the brain, the striatum, may cause the disorder. Differences in other parts of the brain and an imbalance of brain chemicals, especially serotonin and dopamine, may also contribute to OCD. Independent studies have consistently found unusual dopamine and serotonin activity in various regions of the brain in individuals with OCD. These can be defined as dopaminergic hyperfunction in the prefrontal cortex and serotonergic hypofunction in the basal ganglia.

## *Diagnosis*

Formal diagnosis may be performed by a psychologist, psychiatrist, clinical social worker, or other licensed mental health professional. To be diagnosed with OCD, a person must have obsessions, compulsions, or both, according to the Diagnostic and Statistical Manual of Mental Disorders (DSM). The Quick Reference to the 2000 edition of the DSM suggests that several features characterize clinically significant obsessions and compulsions. Such obsessions, the DSM says, are recurrent and persistent thoughts, impulses, or images that are experienced as intrusive and that cause marked anxiety or distress. These thoughts, impulses, or images are of a degree or type that lies outside the normal range of worries about conventional problems. A person may attempt to ignore or suppress such obsessions, or to neutralize them with some other thought or action, and will tend to recognize the obsessions as idiosyncratic or irrational.

Compulsions become clinically significant when a person feels driven to perform them in response to an obsession, or according to rules that must be applied rigidly, and when the person consequently feels or causes significant distress. Therefore, while many people who do not suffer from OCD may perform actions often associated with OCD (such as ordering items in a pantry by height), the distinction with clinically significant OCD lies in the fact that the person who suffers from OCD *must* perform these actions, otherwise they will experience significant psychological distress. These behaviors or mental acts are aimed at preventing or reducing distress or preventing some dreaded event or situation;

however, these activities are not logically or practically connected to the issue, or they are excessive. In addition, at some point during the course of the disorder, the individual must realize that their obsessions or compulsions are unreasonable or excessive. Moreover, the obsessions or compulsions must be time-consuming (taking up more than one hour per day) or cause impairment in social, occupational, or scholastic functioning. It is helpful to quantify the severity of symptoms and impairment before and during treatment for OCD. In addition to the patient's estimate of the time spent each day harboring obsessive-compulsive thoughts or behaviors, Fenske and Schwenk in their article "Obsessive-Compulsive Disorder: Diagnosis and Management," argue that more concrete tools should be used to gauge the patient's condition (2009). This may be done with rating scales, such as the most trusted Yale–Brown Obsessive Compulsive Scale (Y-BOCS). With measurements like these, psychiatric consultation can be more appropriately determined because it has been standardized.

## Differential diagnosis

OCD is often confused with the separate condition obsessive–compulsive personality disorder. OCD is *ego dystonic*, meaning that the disorder is incompatible with the sufferer's self-concept. Because disorders that are ego dystonic go against a person's self-concept, they tend to cause much distress. OCPD, on the other hand, is *ego syntonic*—marked by the person's acceptance that the characteristics displayed as a result of this disorder are compatible with his or her self-image.

People with OCD are often aware that their behavior is not rational and are unhappy about their obsessions but nevertheless feel compelled by them. People with OCPD are not aware of anything abnormal about themselves; they will readily explain why their actions are rational, and it is usually impossible to convince them otherwise.

People with OCD are ridden with anxiety; by contrast, people with OCPD tend to derive pleasure from their obsessions or compulsions.

Some OCD sufferers exhibit what is known as *overvalued ideas*. In such cases, the person with OCD will truly be uncertain whether the fears that cause them to perform their compulsions are irrational or not. After some discussion, it is possible to convince the individual that their fears may be unfounded. It may be more difficult to do ERP therapy on such patients because they may be unwilling to cooperate, at least initially. For this reason OCD has often been likened to a disease of pathological doubt, in which the sufferer, though not usually delusional, is often unable to realize fully which dreaded events are reasonably possible and which are not. There are severe cases in which the sufferer has an unshakeable belief in the context of OCD that is difficult to differentiate from psychosis.

OCD is different from behaviors such as gambling addiction and overeating. People with these disorders typically experience at least some pleasure from their activity; OCD sufferers do not actively want to perform their compulsive tasks and experience no pleasure from doing so.

OCD can, like many forms of chronic stress, lead to clinical depression over time. The constant stress of the condition can cause sufferers to develop a deadening of spirit, a numbing frustration, or sense of hopelessness. OCD's effects on day-to-day life, particularly its substantial consumption of time, can produce difficulties with work, finances, and relationships. There is no known cure for OCD, but a number of successful treatment options are available.

## *Management*

According to a team of Duke University-led psychiatrists, behavioral therapy (BT), cognitive behavioral therapy (CBT), and medications should be regarded as first-line treatments for OCD. Psychodynamic psychotherapy may help in managing some aspects of the disorder. The American Psychiatric Association notes a lack of controlled demonstrations that psychoanalysis or dynamic psychotherapy is effective "in dealing with the core symptoms of OCD."

### Behavioral therapy

The specific technique used in BT/CBT is called exposure and ritual prevention (also known as "exposure and response prevention") or ERP; this involves gradually learning to tolerate the anxiety associated with not performing the ritual behavior. At first, for example, someone might touch something only very mildly "contaminated" (such as a tissue that has been touched by another tissue that has been touched by the end of a toothpick that has touched a book that came from a "contaminated" location, such as a school.) That is the "exposure". The "ritual prevention" is not washing. Another example might be leaving the house and checking the lock only once (exposure) without going back and checking again (ritual prevention). The person fairly quickly habituates to the anxiety-producing situation and discovers that their anxiety level has dropped considerably; they can then progress to touching something more "contaminated" or not checking the lock at all—again, without performing the ritual behavior of washing or checking.

Exposure ritual/response prevention (ERP) has a strong evidence base. It is generally considered the most effective treatment for OCD.

It has generally been accepted that psychotherapy, in combination with psychotropic medication, is more effective than either option alone. However, more recent studies have shown no difference in outcomes for those treated with the combination of medicine and CBT versus CBT alone.

More recent behavioral work has focused on *associative splitting*. It is a new technique aimed at reducing obsessive thoughts. The method draws upon the “fan effect” of associative priming: The sprouting of new associations diminishes the strength of existing ones. As OCD patients show marked biases or restrictions in OCD-related semantic networks (e.g., cancer is only associated with “illness” or “death”, fire is only associated with “danger” or “destruction”), they are encouraged to imagine neutral or

positive associations to OCD-related cognitions (cancer = zodiac sign, animal, crab; fire = fireflies, fireworks, candlelight-dinner). First studies tentatively confirm the feasibility and effectiveness of the approach for a subgroup of patients.

## Medication

Medications as treatment include selective serotonin reuptake inhibitors (SSRIs) such as paroxetine, sertraline, fluoxetine, escitalopram and fluvoxamine and the tricyclic antidepressants, in particular clomipramine. SSRIs prevent excess serotonin from being pumped back into the original neuron that released it. Instead, serotonin can then bind to the receptor sites of nearby neurons and send chemical messages or signals that can help regulate the excessive anxiety and obsessive thoughts. In some treatment-resistant cases, a combination of clomipramine and an SSRI has shown to be effective even when neither drug on its own has been efficacious.

Treatment of OCD is an area needing significant improvement in prescribing regimens. Benzodiazepines are sometimes used, although they are generally believed to be ineffective for treating OCD; however, effectiveness was found in one small study. Serotonergic antidepressants typically take longer to show benefit in OCD than with most other disorders they are used to treat. It is common for 2–3 months to elapse before any tangible improvement is noticed. In addition to this, treatment usually requires high dosages. Fluoxetine, for example, is usually prescribed in dosages of 20 mg per day for clinical depression, whereas with OCD the dosage often ranges from 20 mg to 80 mg or higher, if necessary. In most cases antidepressant therapy alone provides only a partial reduction in symptoms, even in cases that are not deemed treatment resistant. Much current research is devoted to the therapeutic potential of the agents that affect the release of the neurotransmitter glutamate or the binding to its receptors. These include riluzole, memantine, gabapentin, N-Acetylcysteine, and lamotrigine. MDMA, which is a powerful and illicit serotonergic drug, has also been anecdotally reported to temporarily alleviate the symptoms of OCD.

The atypical antipsychotics olanzapine, quetiapine, and risperidone have also been found to be useful as adjuncts to an SSRI in treatment-resistant OCD. However, these drugs are often poorly tolerated, and have significant metabolic side effects that limit their use. None of the atypical antipsychotics have demonstrated efficacy as a monotherapy.

## Experimental drug treatments

The naturally occurring sugar inositol has been suggested as a treatment for OCD, as it appears to modulate the actions of serotonin and reverse desensitisation of neurotransmitter receptors.

Nutrition deficiencies may also contribute to OCD and other mental disorders. Vitamin and mineral supplements may aid in such disorders and provide nutrients necessary for proper mental functioning.

μ-Opioids, such as hydrocodone and tramadol, may rapidly ameliorate OCD symptoms. Tramadol is an atypical opioid that appears to provide the anti-OCD effects of an opiate and inhibit the re-uptake of serotonin (in addition to norepinephrine) Oral morphine, administered once weekly, has been shown to reduce OCD symptoms in some treatment-resistant patients. The mechanism of therapeutic action is unknown. Administration of opiate treatment may be contraindicated in individuals concurrently taking CYP2D6 inhibitors such as fluoxetine and paroxetine.

Psychedelics such as LSD, peyote, and tryptamine alkaloid psilocybin have been proposed as treatment due to their observed effects on OCD symptoms. It has been hypothesised that hallucinogens may stimulate 5-HT2A receptors and, less significantly, 5-HT2C receptors, causing an inhibitory effect on the orbitofrontal cortex, an area of the brain strongly associated with hyperactivity and OCD.

Regular nicotine treatment may ameliorate symptoms of OCD, although the pharmacodynamical mechanism by which this is achieved is not yet known, and more detailed studies are needed to fully confirm this hypothesis.

Because of choline's anti-dopaminergic effects often worsen OCD symptoms, anticholinergics are sometimes used as a supplementary treatment for OCD symptoms.

St John's Wort was previously believed to be of benefit due to its (non-selective) serotonin re-uptake inhibiting qualities, but a double-blind study using a flexible-dose schedule (600–1800 mg/day) found no difference between St John's Wort and a placebo.

## Electroconvulsive therapy (ECT)

Electroconvulsive therapy (ECT) has been found effective in severe and refractory cases.

## Psychosurgery

For some, neither medication, support groups nor psychological treatments are helpful in alleviating obsessive–compulsive symptoms. These patients may choose to undergo psychosurgery as a last resort. In this procedure, a surgical lesion is made in an area of the brain (the cingulate cortex). In one study, 30% of participants benefited significantly from this procedure. Deep-brain stimulation and vagus nerve stimulation are possible surgical options that do not require destruction of brain tissue. In the US, the Food and Drug Administration approved deep-brain stimulation for the treatment of OCD under a humanitarian device exemption requiring that the procedure be performed only in a hospital with specialist qualifications to do so.

In the US, psychosurgery for OCD is a treatment of last resort and will not be performed until the patient has failed several attempts at medication (at the full dosage) with augmentation, and many months of intensive cognitive–behavioral therapy with exposure and ritual/response prevention. Likewise, in the UK, psychosurgery cannot be performed

unless a course of treatment from a suitably qualified cognitive–behavioral therapist has been carried out.

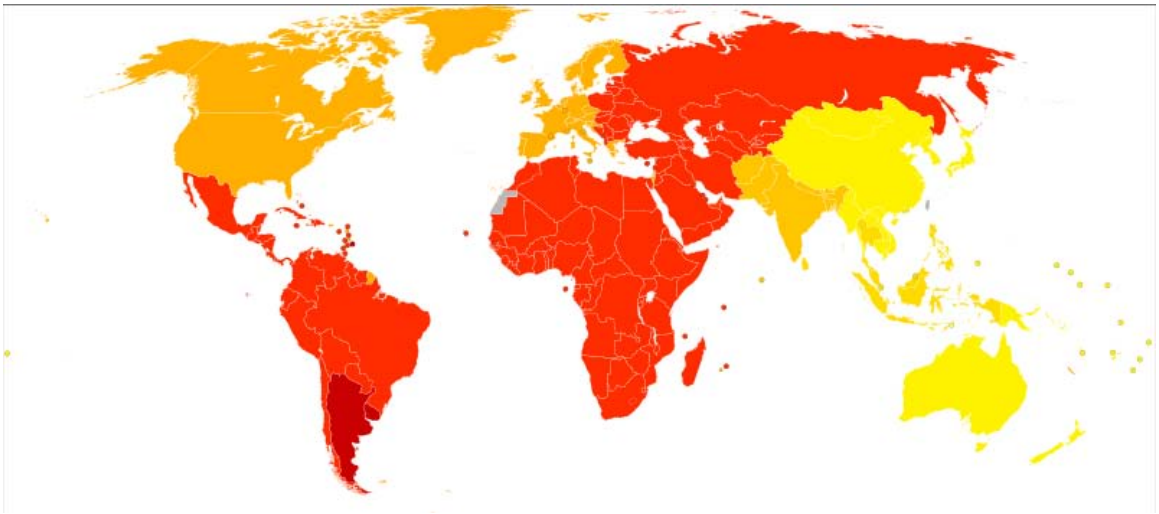
### Treatment in children and adolescents

Therapeutic treatment may be effective in reducing ritual behaviors of OCD for children and adolescents. Family involvement, in the form of behavioral observations and reports, is a key component to the success of such treatments. Parental intervention also provides positive reinforcement for a child who exhibits appropriate behaviors as alternatives to compulsive responses. After one or two years of therapy, in which a child learns the nature of his or her obsession and acquires strategies for coping, that child may acquire a larger circle of friends, exhibit less shyness, and become less self-critical.

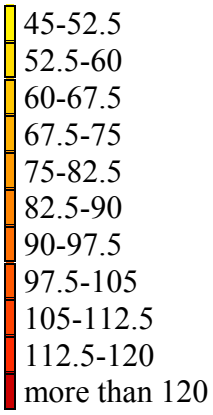
Although the causes of OCD in younger age groups range from brain abnormalities to psychological preoccupations, life stress such as bullying and traumatic familial deaths may also contribute to childhood cases of OCD, and acknowledging these stressors can play an role in treating the disorder.

The mental technique of "thought stopping" can help reduce or eliminate obsessive thoughts. In this procedure, whenever an individual has an obsessive thought, he or she is encouraged to utter "STOP" in mid-thought to interrupt the obsession. A variant of the process avoids making the word "STOP" a stimulus to the obsessive thoughts: in the presence of an obsessive thought, a child counts loudly backward from ten, and then evokes a pleasant scene.

## *Epidemiology*



Disability-adjusted life year for obsessive-compulsive disorder per 100,000 inhabitants in 2002.
no data
less than 45




OCD does not have a higher affinity for a specific gender. In 80% of cases, symptoms present before the child is 18 years old. Studies have placed the prevalence between one and three percent, although the prevalence of clinically recognized OCD is much lower, suggesting that many individuals with the disorder may not be diagnosed. The fact that many individuals do not seek treatment may be due in part to stigma associated with OCD.

In a 1980 study of adults from several U.S. cities, the lifetime prevalence rate of OCD for both sexes was recorded at 2.5 percent. Education also appears to be a factor. The lifetime prevalence of OCD is lower for those who have graduated from high school than for those who have not (1.9 percent versus 3.4 percent). However, in the case of college education, lifetime prevalence is higher for those who graduate with a degree (3.1 percent) than it is for those who have only some college background (2.4 percent). As far as age is concerned, the onset of OCD usually ranges from the late teenage years until the mid-20s in both sexes, but the age of onset tends to be slightly younger in males than in females.

A study suggests that OCD symptoms in Japanese patients are similar to those found in Western countries, suggesting that this disorder transcends culture and geography. The study, published in 2008, appears to contradict previous theories, said the study's lead author, Hisato Matsunaga. Having "hypothesized that symptom structure might be substantially influenced by the sociocultural differences", Hisato said that he was surprised by the results.

It has been proposed that sufferers are generally of above-average intelligence, as the very nature of the disorder necessitates complicated thinking patterns.

## Comorbidity

People with OCD may be diagnosed with other conditions, such as major depressive disorder, generalized anxiety disorder, anorexia nervosa, social anxiety disorder, bulimia nervosa, Tourette syndrome, Asperger syndrome, compulsive skin picking, body dysmorphic disorder, trichotillomania, and (as already mentioned) obsessive–compulsive personality disorder. There is some research demonstrating a link between drug addiction

and OCD as well. Many who suffer from OCD also suffer from panic attacks. There is a higher risk of drug addiction among those with any anxiety disorder (possibly as a way of coping with the heightened levels of anxiety), but drug addiction among OCD patients may serve as a type of compulsive behavior and not just as a coping mechanism. Depression is also extremely prevalent among sufferers of OCD. One explanation for the high depression rate among OCD populations was posited by Mineka, Watson, and Clark (1998), who explained that people with OCD (or any other anxiety disorder) may feel depressed because of an "out of control" type of feeling. In further consideration of OCD comorbidities, the research of Fenske and Schwenk reports that studies have shown that depression among those with OCD is particularly alarming because their risk of suicide is high; more than 50 percent of patients experience suicidal tendencies, and 15 percent have attempted suicide. Individuals with OCD have also been found to be affected by delayed sleep phase syndrome at a substantially higher rate than the general public.

## *Prognosis*

Psychological interventions such as behavioral and cognitive-behavioral therapy as well as pharmacological treatment can lead to substantial reduction of OCD symptoms for the average patient. However, OCD symptoms persist at moderate levels even following adequate treatment course and a completely symptom-free period is uncommon.

### Cognitive performance

OCD is associated with higher IQ.

A 2009 study that conducted "a battery of neuropsychological tasks to assess nine cognitive domains with a special focus on executive functions concluded that "few neuropsychological differences emerged between the OCD and healthy participants when concomitant factors were controlled."

## *History*

From the 14th to the 16th century in Europe, it was believed that people who experienced blasphemous, sexual, or other obsessive thoughts were possessed by the Devil. Based on this reasoning, treatment involved banishing the "evil" from the "possessed" person through exorcism. In the early 1910s, Sigmund Freud attributed obsessive–compulsive behavior to unconscious conflicts that manifest as symptoms. Freud describes the clinical history of a typical case of "touching phobia" as starting in early childhood, when the person has a strong desire to touch an item. In response, the person develops an "external prohibition" against this type of touching. However, this "prohibition does not succeed in abolishing" the desire to touch; all it can do is repress the desire and "force it into the unconscious".

# Chapter 16

# Adult Attention Deficit Hyperactivity Disorder

**Adult attention deficit hyperactivity disorder** (also referred to as **Adult ADHD**, **Adult ADD**) is the common term used to describe the neuropsychiatric condition attention-deficit hyperactivity disorder (ADHD) when it is present in adults. Up to 60% of children diagnosed with ADHD in early childhood continue to demonstrate notable ADHD symptoms as adults. Current convention refers to this condition as adult ADHD, according to the Diagnostic & Statistical Manual for Mental Disorders (DSM-IV-TR), 2000 revision. It has been estimated that 5% of the global population has ADHD (including cases not yet diagnosed).

Successful treatment of ADHD is usually based on a combination of medication, behavior therapy, cognitive therapy, and skills training.

## *Classification*

The DSM-IV, or Diagnostic and Statistical Manual of Mental Disorders, 2000 edition, defines three types of ADHD:

1) An *inattentive* type
2) A *hyperactive/impulsive* type
3) A *combined* type

To meet the formal diagnostic criteria of ADHD, an individual must display:

at least six inattentive-type symptoms for the inattentive-type
at least six hyperactive-type symptoms for the hyperactive/impulsive type
all of the above to have the combined-type

The symptoms need to have been present since before the individual was seven years old, and must have interfered with at least two spheres of his or her functioning (at home and at school or work, for example) over the last six months.

## *Signs and symptoms*

Individuals with ADHD have deficiencies with self-regulation and self-motivation, that cause problems with distractibility, procrastination, organization, and prioritization. The learning potential and overall intelligence of an adult with ADHD, however, are no different from the potential and intelligence of adults who do not have the disorder. ADHD is a chronic condition, beginning in early childhood and persisting throughout a person's lifetime. It is estimated that up to 60% of children with ADHD will continue to have significant ADHD-related symptoms persisting into adulthood, resulting in a significant impact on education, employment, and interpersonal relationships.

Whereas teachers and caregivers responsible for children are often attuned to the symptoms of ADHD, employers and others who interact with adults are far less likely to regard such behaviors as a symptom. In part, this is because symptoms do change with maturity; adults who have ADHD are less likely to exhibit obvious hyperactive behaviors. Research shows that adults with ADHD are more likely than their non-ADHD counterparts to experience automobile accidents and less likely to complete their education. ADHD adults have significantly lower rates of professional employment, even controlling for confounding psychiatric problems.

Adults with ADHD are often perceived by others as chaotic and disorganized, with a tendency to need high stimulation to be less distracted and function effectively. As their coping mechanisms become overwhelmed, some individuals may turn to smoking, alcohol, or illicit drugs. As a result, many adults suffer from associated or "co-morbid" psychiatric conditions such as depression, anxiety, or substance abuse. Many with ADHD also have associated learning disabilities, such as dyslexia, which contributes to their difficulties.

**Inattentive-type (ADHD-I)**

In **children**:

- Forgetful during daily activities
- Easily distracted by extraneous stimuli
- Losing important items (e.g. pencils, homework, toys, etc.)
- Not listening and not responding to name being called out
- Unable to focus on tasks at hand, cannot sustain attention in activities
- Avoids or dislikes tasks requiring sustained mental effort
- Makes careless mistakes by failing to pay attention to details
- Difficulty organizing tasks and activities
- Fails to follow-through on complex

**Hyperactive/Impulsive-type (ADHD-H)**

In **children**:

- Squirms and fidgets (with hands and/or feet)
- Cannot sit still
- Cannot play quietly or engage in leisurely activities
- Talks excessively
- Runs and climbs excessively
- Always on the go, as if "driven by a motor"
- Cannot wait for their turn
- Blurts out answers
- Intrudes on others and interrupts conversations

instructions and tasks (e.g. homework, chores, etc.)

In **adults**, these evolve into:

- Procrastination
- Indecision, difficulty recalling and organizing details required for a task
- Poor time management, losing track of time
- Avoiding tasks or jobs that require sustained attention
- Difficulty initiating tasks
- Difficulty completing and following through on tasks
- Difficulty multitasking
- Difficulty shifting attention from one task to another

In **adults**:

- Chooses highly active, stimulating jobs
- Avoids situations with low physical activity or sedentary work
- May choose to work long hours or two jobs
- Seeks constant activity
- Easily bored
- Impatient
- Intolerant to frustration, easily irritated
- Impulsive, snap decisions and irresponsible behaviors
- Loses temper easily, angers quickly

Most adults with ADHD have the inattentive-type, but men exhibit a tendency towards the hyperactive/impulsive-type symptoms and have predominantly the combined-type. Symptoms of ADHD can vary widely between individuals and throughout the lifetime of an individual. As the neurobiology of ADHD is becoming increasingly understood, it is becoming evident that difficulties exhibited by individuals with ADHD are due to problems with the brain known as executive functioning. These result in problems with sustaining attention, planning, organizing, prioritizing, and impulsive thinking/decision making. These symptoms are independent of an individual's overall intelligence.

The difficulties generated by these symptoms can range from moderate to extreme. Inability to effectively structure their lives, plan simple daily tasks, or think of consequences results in various difficulties: poor performance in school and work leading to academic underachievement or getting fired, poor driving record with traffic violations and accidents, multiple relationships or serial marriages, legal problems, sexually-transmitted diseases, unplanned pregnancies, smoking, alcoholism, substance abuse. As problems accumulate, a negativistic self-view becomes established and a vicious circle of failure is set up. Up to 80% of adults may have some form of psychiatric comorbidity. The difficulty is often due to the ADHD person's observed behaviour (e.g. the impulsive types, who may insult their boss for instance, resulting in dismissal), despite genuinely trying to avoid these and knowing that it can get them in trouble. Often, the ADHD person will miss things that an adult of similar age and experience should catch onto or know. These lapses can lead others to label the individuals with ADHD as "lazy" or "stupid" or "inconsiderate".

Ultimately, this constellation of symptoms can be summarized as a deficiency in self-regulation and self-motivation, especially for the impulsive/hyperactive types. Assessment of adult patients seeking a possible diagnosis can be better than in children due to the adult's greater ability to provide their own history, input, and insight. However, it has been noted that many individuals, particularly those with high intelligence, develop coping strategies that mask ADHD impairments and therefore they do not present for diagnosis and treatment.

## *Diagnosis*

The diagnosis of ADHD in adults is entirely a clinical one, which contributes to controversy. It requires retrospectively establishing whether the symptoms were also present in childhood, even if not previously recognized. There is no objective "test" that diagnoses ADHD. Rather, it is a combination of a careful history of symptoms up to early childhood, including corroborating evidence from family members, previous report cards, etc. along with a neuropsychiatric evaluation. The neuropsychiatric evaluation often includes a battery of tests to assess overall intelligence and general knowledge, self-reported ADHD symptoms, ADHD symptoms reported by others, and tests to screen for co-morbid conditions. Some of these include, but are not limited to the WAIS, BADDS, and/or WURS tests in order to have some objective evidence of ADHD. The screening tests also seek to rule out other conditions or differential diagnoses such as depression, anxiety, or substance abuse. "Organic" diseases such as hyperthyroidism may also present with symptoms similar to those of ADHD, and it is imperative to rule these out as well. Asperger syndrome, a condition on the autism spectrum, is sometimes mistaken for ADHD, due to impairments in executive functioning found in some people with Asperger syndrome. However, Asperger syndrome also typically involves difficulties in social interaction, restricted and repetitive patterns of behavior and interests, and problems with sensory integration, including hypersensitivity.

Generally, medical and mental health professionals follow the Diagnostic and Statistical Manual of Mental Disorders (DSM) of the American Psychiatric Association. Periodic updates to the DSM incorporate changes in knowledge and treatments. Under the DSM-IV (published in 1994, with corrections and minor changes in 2000), the diagnostic criteria for ADHD in adults follow the same as in children. The proposed revision for the DSM-5 differentiates the presentation of ADHD for children and adults for several symptoms DSM-5 ADHD.

It should be noted that every normal individual exhibits ADHD-like symptoms occasionally (when tired or stressed, for example) but to have the diagnosis, the symptoms should be present from childhood and persistently interfere with functioning in multiple spheres of an individual's life: work, school, and interpersonal relationships. The symptoms that individuals exhibit as children are still present in adulthood, but manifest differently as most adults develop compensatory mechanisms to adapt to their environment.

## *Pathophysiology*

Over the last 10 years, research into ADHD has greatly accelerated. There is no single, unified theory that explains the cause of ADHD and research is ongoing.

It is becoming increasingly accepted that individuals with ADHD have difficulty with what neuropsychologists term "executive functioning". In higher organisms, such as humans, these functions are thought to reside in the frontal lobes. They enable us to recall tasks that need accomplishing, organize ourselves to accomplish these tasks, assess the consequences of actions, prioritize thoughts and actions, keep track of time, be aware of our interaction with our surroundings, sort out competing stimuli, and adapt to changing situations. They also enable us to judge what is "right" or "correct" as opposed to what is "wrong" or "incorrect".

(Phineas Gage, a railroad worker who in 1848 survived a large iron rod being accidentally driven through his head, is often cited as a demonstration that executive function resides in the frontal lobes, because at least one of those lobes was destroyed in Gage by the accident, after which his behavior and personality were markedly changed. However, while Gage's case certainly stimulated 19th-century thinking about the brain and the localization of its functions, most specific uses of Gage to illustrate theoretical ideas about the brain employ greatly exaggerated descriptions of his behavioral changes.)

The executive functions of the brain in the frontal lobes are thought to be linked to the rest of the brain by way of the prefrontal cortex. This part of the brain is involved in working memory and linked to the limbic system, which controls our basic emotions of fear, anger, pleasure and also plays an important role in the formation of long-term memories. The nucleus accumbens is a part of the brain that is involved in our internal reward system and allows us to feel pleasure, success, or accomplishments in response to certain stimuli. Many of these interconnections are via dopaminergic pathways. For example, cocaine and amphetamines act directly on this part of the brain to stimulate dopamine release, giving users a euphoric feeling.

Several lines of research based on structural and/or functional imaging techniques, stimulant drugs, psychological interventions have identified alterations in the dopaminergic and adrenergic pathways of individuals with ADHD. In particular, areas of the prefrontal cortex appear to be the most affected. Dopamine and norepinephrine are neurotransmitters playing an important role in brain function. The uptake transporters for dopamine and norepinephrine are overly active and clear these neurotransmitters from the synapse a lot faster than in normal individuals. This is thought to increase processing latency, diminishes working memory, and affects salience. To make an analogy, individuals with ADHD have a problem with the search engine of their brain—the "raw" data (knowledge) is all stored in the cortex, but accessing it, prioritizing it, synthesizing it, and keeping it all in mind is problematic.

Stimulants, such as methylphenidate and amphetamine act on these neurons to increase the availability of dopamine and norepinephrine for neurotransmission. They act to

correct the problem with the "wiring". Methylphenidate acts by blocking the dopamine and norepinephrine transporters, thus slowing the pace at which these neurotransmitters are cleared from the synapse. Amphetamine acts in a similar fashion, but also increases the release of these neurotransmitters into the synaptic cleft by temporarily reversing the uptake process.

## *Treatment*

Stimulant medication is a common and effective treatment for Adult ADHD although the response rate may be lower for adults than children. The non-stimulant Atomoxetine is also an effective treatment for adult ADHD, but without the abuse potential of stimulant medication but has been associated with increased incidence of suicidal thoughts. Some physicians may recommend antidepressant drugs instead of stimulants, though antidepressants have lower treatment effect sizes than stimulant medication.

Treatment for adult ADHD may combine medication and behavioral, cognitive, or vocational interventions. Treatment often begins with medication selected to address the symptoms of ADHD, along with any comorbid conditions that may be present. Medication alone, while effective in correcting the physiological symptoms of ADHD, will not address the paucity of skills which many adults will have failed to acquire because of their ADHD (e.g., one might regain *ability* to focus with medication, but skills such as organizing, prioritizing and effectively communicating have taken others time to cultivate).

### Psychosocial therapy

Treatment of adult ADHD may also include forms of anxiety or stress management.

Research has shown that, alongside medication, brief psychological interventions in adults can be effective in reducing symptomatic deficiencies. Although cognitive behavioral therapy has not proven effective in children with ADHD, it may be helpful in adults.

### Medications

Stimulant medications are often the first line of treatment and are effective in approximately 80% of individuals. When stimulants are prescribed, low doses are generally recommended for adults with ADHD. High doses of stimulants offer no additional benefit and increase adverse effects. Stimulants are formulated in short-acting, immediate-acting, or long-acting formulations. There is always abuse potential, especially with the short-acting forms which can potentially be injected or snorted which is why long-acting formulations are recommended. Many of these long-acting formulations prevent them from being injected or snorted. In adults, stimulants may increase the risk of adverse cardiovascular events such as myocardial infarctions (heart attacks) or hypertension (high blood pressure). Judicious use and careful, regular follow-up with a physician are therefore critically important.

The stimulant methylphenidate (or MPH) is often the first-line therapy. In the short term, methylphenidate is well tolerated however long term safety has not been determined in adults and there are concerns about increases in blood pressure in those treated. Again, careful discussion with the treating physician and good clinical judgment are important to decide on the most appropriate therapy.

Amphetamines and their derivatives are also effective in the treatment of adult ADHD. They not only block the uptake of dopamine and norepinephrine, but increase the release of these from the pre-synaptic neuron. They may have a better side-effect profile than methylphenidate, especially in terms of cardiovascular events, and are potentially better tolerated.

Non-stimulant medication, such as atomoxetine, acts by inhibiting the norepinephrine transporter. It is often prescribed in adults who cannot tolerate the side effects of amphetamines or methylphenidate. It is also effective and approved by the FDA (Food and Drug Administration). A rare but potentially severe side effect includes liver damage and increased suicidal ideation. These should be discussed with the prescribing physician.

### Neurofeedback

Efficacy of neurofeedback in treating attentional deficit in adults has been demonstrated in an outcome study. Research has also shown that neurofeedback outcomes compare favorably to those of stimulant medications.

## *Epidemiology*

In North America and Europe, it is estimated that three to five percent of adults have ADHD, but only about ten percent of those have received a formal diagnosis. In the context of the World Health Organization World Mental Health Survey Initiative, researchers screened more than 11,000 people aged 18 to 44 years in ten countries in the Americas, Europe and the Middle East. On this basis they estimated the adult ADHD proportion of the population to average 3.5 percent with a range of 1.2 to 7.3 percent, with a significantly lower prevalence in low-income countries (1.9%) compared to high-income countries (4.2%). The researchers concluded that adult ADHD often co-occurs with other disorders, and that it is associated with considerable role disability. Although they found that few adults are treated for ADHD itself, in many instances treatment is given for the co-occurring disorders.

## *History*

In the 1970s researchers began to realize that the condition now known as ADHD did not always disappear in adolescence, as was once thought. At about the same time, some of the symptoms were also noted in many parents of the children under treatment. The condition was formally recognized as afflicting adults in 1978, often informally called *adult ADD*, since symptoms associated with hyperactivity are generally less pronounced.

## *Societal Impact*

ADHD in adults, as with children, is recognized as an impairment that may constitute a disability under U.S. federal disability nondiscrimination laws, including such laws as the Rehabilitation Act of 1973 and the Americans With Disabilities Act (ADA, 2008 revision), if the disorder substantially limits one or more of an individual's major life activities. For adults whose ADHD does constitute a disability, workplaces have a duty to provide reasonable accommodations, and educational institutions have a duty to provide appropriate academic adjustments or modifications, to help the individual work more efficiently and productively.

In a 2004 study it was estimated that the yearly income discrepancy for adults with ADHD was $10,791 less per year than high school graduate counterparts and $4,334 lower for college graduate counterparts. The study estimates a total loss in productivity in the United States of over $77 billion USD. By contrast, loss estimations for drug abuse are $58 billion; for alcohol abuse are $85 billion; and for depression are $43 billion.

# Chapter 17

# Diet and Attention Deficit Hyperactivity Disorder

For some children, diet is suspected of playing a role in the multiple behavioral and cognitive symptoms of attention deficit hyperactivity disorder (ADHD). Concerns have focused on food additives, blood sugar regulation, food allergies and intolerances, and vitamin, mineral and fatty acid deficiencies.

## *Additives*

For more than 30 years, questions have been raised about whether the synthetic dyes, flavors, and preservatives found in many commercially prepared and "junk" foods might contribute to hyperactivity or other symptoms of ADHD. Traditional research found limited support for diets like the Feingold diet, which eliminates certain processed foods and food additives as well as certain fruits and vegetables.

In September 2007, research financed by Britain's Food Standards Agency and published online by the British medical journal *The Lancet* presented evidence that a mix of additives commonly found in children's foods increases the mean level of hyperactivity.

The team of researchers concluded that "the finding lends strong support for the case that food additives exacerbate hyperactive behaviors (inattention, impulsivity and overactivity) at least into middle childhood." That study examined the effect of artificial colors and a sodium benzoate preservative, and found both to be problematic for some children. Further studies are needed to find out whether there are other additives that could have a similar effect, and it is unclear whether some disturbances can also occur in mood and concentration in some adults. In the February 2008 issue of its publication, *AAP Grand Rounds*, the American Academy of Pediatrics concluded that a low-additive diet is a valid intervention for children with ADHD:

Although quite complicated, this was a carefully conducted study in which the investigators went to great lengths to eliminate bias and to rigorously measure outcomes. The results are hard to follow and somewhat inconsistent. For many of the assessments there were small but statistically significant differences of measured behaviors in children who consumed the food additives compared with those who did not. In each case increased hyperactive behaviors were associated with consuming the additives. For those

comparisons in which no statistically significant differences were found, there was a trend for more hyperactive behaviors associated with the food additive drink in virtually every assessment. Thus, the overall findings of the study are clear and require that even we skeptics, who have long doubted parental claims of the effects of various foods on the behavior of their children, admit we might have been wrong.

Several other recent studies have renewed interest in whether certain foods and additives might affect particular symptoms in a subset of children with ADHD.

As of mid-2009, the consensus on a sensible approach to nutrition for children with ADHD is the same recommended for all children: *eat a diet that emphasizes fruits and vegetables, whole grains, healthful unsaturated fats, and good sources of protein; go easy on unhealthy saturated and trans fats, rapidly digested carbohydrates, and fast food; and balance healthy eating with plenty of physical activity*. (Emphasis added)

As yet there is no consensus about how such additives might contribute to ADHD symptoms in children. In a recent well-designed study in Britain, the investigators found a mild but significant increase in hyperactivity in both age groups of children—across the board, regardless of baseline hyperactivity levels—during the weeks when they consumed drinks containing artificial colors. This study concluded that the additives might explain about 10% of the behavioral difference between a child with ADHD and one without the disorder.

An earlier meta-analysis conducted at Columbia University and Harvard University suggests that removing these agents from the diets of children with ADHD would be about one-third to one-half as effective as treatment with methylphenidate (Ritalin).

Authors of both of these studies cautioned that only a minority of children are particularly vulnerable to the effects of artificial additives. They also pointed out that determining which children are susceptible is difficult, though not impossible.

The European Food Safety Authority (EFSA) reviewed the literature on the association between food additives and hyperactivity and concluded that there is only limited evidence of an association between the intake of additives and activity and attention and then only in some children studied. They further indicated that the effects reported in the study were not consistent for the two age groups and for the two food additive mixtures used in the study. Others have suggested a trial of removing additives from the diet for children with ADHD as it is harmless and might be helpful.

## *Sugar regulation*

A number of studies have found that sucrose (sugar) has no effect on behavior and in particular it does not exacerbate the symptoms of children diagnosed with ADHD. One study demonstrated the impact of expectancy effects in parents' perceptions of their children's hyperactivity after consuming sugar. In this study, parents who were told their child had ingested a high concentration of sugar in drink form (even though the drink was

actually flavored with aspartame), reported their child as being more active, inattentive and resistant to parental demands. This was in comparison to the group who were told (accurately) that their child had ingested no sugar.

## *Omega-3 fatty acids*

Some research suggests that children with ADHD may have low blood levels of essential omega-3 fatty acids. However, it is unknown if decreased blood levels of omega-3 fatty acids can cause or exacerbate ADHD or whether lower blood levels of omega-3 fatty acids associated with ADHD are caused by an underlying mechanism. Fish oils appear to reduce ADHD-related symptoms in some children. A double blind study has showed "medium to strong treatment effects of omega 3 fatty acids on symptoms of ADHD" after administering amounts around 1 gram for three to six months.

# Chapter 18

# Attention-Deficit Hyperactivity Disorder Management

**Attention-deficit/hyperactivity disorder management** are the treatment options available to people with attention-deficit/hyperactivity disorder (ADHD).

There are several effective and clinically proven options to treat people with ADHD. Combined medical management and behavioral treatment is the most effective ADHD management strategy, followed by medication alone, and then behavioral treatment. However, these results have been questioned because the study from the multimodal treatment group faded the behavioral procedure 3 months prior to the last evaluation point but continued the medication group. Indeed, after 14 months the medication group lost its advantage to the long discontinued behavior modification group. By year eight socioeconomic status and family structure were the only predictive varibale for ADHD treatment

The most common stimulant medications are methylphenidate (Ritalin), dextroamphetamine (Dexedrine), and mixed amphetamine salts (Adderall). Atomoxetine (Strattera) is currently the only non-stimulant drug approved for the treatment of ADHD. Other medications which may be prescribed off-label include certain antidepressants such as tricyclic antidepressants, SNRIs or MAOIs. The presence of comorbid (relating to two diseases that occur together, e.g. depression and ADHD) disorders make finding the right treatment and diagnosis much more costly and time consuming.

## *Effective treatments*

A variety of psychotherapeutic and behavior modification approaches to managing ADHD are employed by psychologists and psychiatrists. These include psychotherapy and working memory therapy. Improving the surrounding home and school environment with parent management training and classroom management can improve the behavior of children with ADHD. Specialized ADHD coaches provide services and strategies to improve functioning, like time management or organizational suggestions. Self control training programs have shown to have limited effectiveness. Behaviorally based self control does better than cognitive self control training A recent meta-analysis found that the use of behavior modification for ADHD resulted in effect sizes in between group

studies (.83), pre-post studies (.70), within group studies (2.64), and single subject studies (3.78) indicating behavioral treatments are highly effective.

Experimental and alternative treatments include nutritional supplements, specialized diets, and biofeedback.

A 2006 meta-analysis of ADHD research concluded that there was a shortage of data regarding ADHD drugs' potential adverse effects, with very few studies assessing the safety or efficacy of treatments beyond four months, and no randomized controlled trials assessing for periods of usage longer than two years. Treatment of preschool children is not recommended. The U.S. Food and Drug Administration (FDA) found that a large number of the controlled trials required subjects who were known to respond to stimulants or who had no history of intolerance to stimulants, and this limits assumed generalizability of the trials' results.

Several studies have found growth and weight suppression for stimulants. Compared to the behavior modification group at 8 years of the government-funded MTA study, the stimulant group had higher level of reported substance abuse.

## *Psychosocial*

There are a variety of psychotherapeutic approaches employed by psychologists and psychiatrists; the one used depends on the patient and the patient's symptoms. The approaches include psychotherapy, cognitive-behavior therapy, support groups, parent training, meditation, and social skills training. If psychotherapy fails to bring improvement medications can be considered as an add-on or alternative.

### Psychotherapy

Psychotherapy is another option, with or without medication, that has been shown to be effective.

### Parent education and classroom management

Improving the surrounding home and school environment can improve the behavior of children with ADHD. Parents of children with ADHD often show similar deficits themselves, and thus may not be able to sufficiently help the child with his or her difficulties. Improving the parents' understanding of the child's behavior and teaching them strategies to improve functioning and communication and discourage unwanted behavior has measurable affect on the children with ADHD. The different educational interventions for the parents are jointly called Parent Management Training. Techniques include operant conditioning: a consistent application of rewards for meeting goals and good behavior (positive reinforcement) and punishments such as time-outs or revocation or privileges for failing to meet goals or poor behavior. Classroom management is similar to parent management training; educators learn about ADHD and techniques to improve

behavior applied to a classroom setting. Strategies utilized include increased structuring of classroom activities, daily feedback, and token economy.

### Working memory training

Many of the problems shown by children with ADHD can be traced back to deficits in working memory (or short-term memory). By training and improving this memory some of the other symptoms may diminish as well. In a study by Klingberg et al., a computerized training program has shown good results in working memory, even if the generalized effect to behavioural symptoms was not as clear.

### Coaching

ADHD Coaching is a specialized type of life coaching that uses specific techniques geared toward working with the unique brain wiring of individuals with attention-deficit/hyperactivity disorder. Professional coaching is not a substitute for traditional, multimodal treatment for ADHD such as medication, diet, exercise, and therapy.

## *Medications*

### Stimulant medication

Stimulants are the most commonly prescribed medications for ADHD. The most common stimulant medications are the chain subsitituted amphetamine methylphenidate (Ritalin, Metadate, Concerta), dexmethylphenidate (Focalin),dextroamphetamine (Dexedrine), mixed amphetamine salts(Adderall), dextromethamphetamine(Desoxyn) and lisdexamfetamine (Vyvanse). However, caution needs to be used when prescribing medications that increase levels of "feel-good" neurotransmitters like dopamine, because they can be addictive. According to several studies, use of stimulants (e.g. methylphenidate) can lead to development of drug tolerance to therapeutic doses; tolerance also occurs among high dose abusers of methylphenidate.

Stimulants used to treat ADHD raise the extracellular concentrations of the neurotransmitters dopamine and norepinephrine which causes an increase in neurotransmission. The therapeutic benefits are due to noradrenergic effects at the locus coeruleus and theprefrontal cortex and dopaminergic effects at the nucleus accumbens.

A meta analysis of clinical trials found that about 70 percent of children improve after being treated with stimulants in the short term but found that this conclusion may be biased due to the high number of low quality clinical trials in the literature. There have been no randomized placebo controlled clinical trials investigating the long term effectiveness of methylphenidate(Ritalin) beyond 4 weeks. Thus the long term effectiveness of methylphenidate has not been scientifically demonstrated. Serious concerns of publication bias regarding the use of methylphenidate for ADHD has also been noted.

Higher rates of schizophrenia and bipolar disorder as well as increased severity of these disorders occur in individuals with a past history of stimulant use for ADHD in childhood. Emergency room visits by children ages 10–14 involving Ritalin intoxication have now reached the same level as those for cocaine which indicates escalating abuse of this highly addictive drug. US and Canada account for a startling 95 percent of worldwide Ritalin consumption. In one study which looked at adult cocaine users, it was found that those individuals who used Ritalin between one and ten years of age had a percentage of cocaine abuse twice that of those who had been diagnosed with ADHD but had not utilized Ritalin.

Both children with and without ADHD abuse stimulants, with ADHD individuals being at the highest risk of abusing or diverting their stimulant prescriptions. Between 16 and 29 percent of students who are prescribed stimulants report diverting their prescriptions. Between 5 and 9 percent of grade/primary and high school children and between 5 and 35 percent of college students have used nonprescribed stimulants. Most often their motivation is to concentrate, improve alertness, "get high," or to experiment.

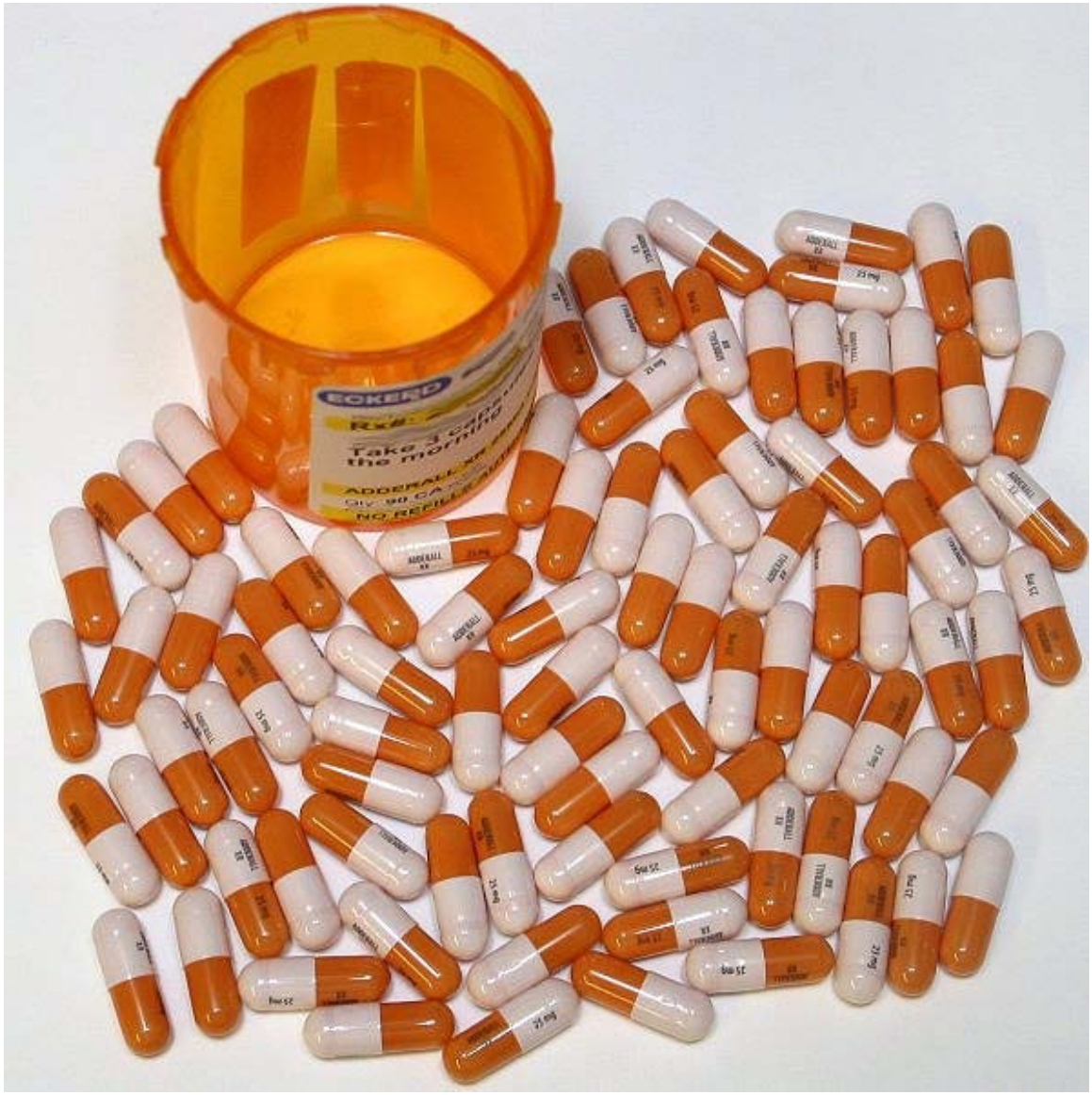
Although one review indicates that long-term use of methylphenidate has potential for abuse and addiction due to its similarity pharmacologically to cocaine and amphetamines. Some other doctors argue that use of stimulant therapy for ADHD does not increase the risk of subsequent substance abuse and may be protective against it when treatment is started in childhood. However, when stimulant therapy is started during adolescence or adulthood, there is an increased risk of subsequent substance abuse.

One study found that children with ADHD actually *need* to move more to maintain the required level of alertness while performing tasks that challenge their working memory. Performing math problems mentally and remembering multi-step directions are examples of tasks that require working memory, which involves remembering and manipulating information for a short time. These findings may also explain why stimulant medications improve the behavior of most children with ADHD. Those medications improve the physiological arousal of children with ADHD, increasing their alertness. Previous studies have shown that stimulant medications temporarily improve working memory abilities.

Although "under medical supervision, stimulant medications are considered safe", the use of stimulant medications for the treatment of ADHD has generated controversy because of undesirable side effects, uncertain long term effects and social and ethical issues regarding their use and dispensation. The U.S. FDA has added black-box warnings to some ADHD medications, while the American Heart Association and theAmerican Academy of Pediatrics feel that it is prudent to carefully assess children for heart conditions before treating them with stimulant medications.

A novel stimulant drug that has been used to treat ADHD is modafinil. There have been double-blind randomized controlled trials that have demonstrated the efficacy and tolerability of modafinil, however there are risks of serious side effects such as skin reactions and modafinil is not recommended for use in children.

## U.S. FDA-approved medicines




Adderall 25 mg XR. Adderall XR is one of the medications used to treat ADHD

Stimulants are the most effective medications available for the treatment of ADHD. Five different formulations of stimulants have been approved by the U.S. Food and Drug Administration (FDA) for the treatment of ADHD: three derived from amphetamine and two derived from methylphenidate. Atomoxetine is the only non-controlled, non-stimulant FDA-approved drug for the treatment of ADHD. There are no differences in effectiveness between medications used for ADHD.

Short term clinical trials have shown medications to be effective for treating ADHD, but the trials usually use exclusion criteria, meaning knowledge on medications for ADHD is based on a small subset of the typical patients seen in clinical practice. They have not been found to improve school performance and data is lacking on long term effectiveness

and the severity of side effects. This class of medicines is generally regarded as one unit; however, they affect the brain differently. Some investigations are dedicated to finding the similarities of children who respond to a specific medicine. The behavioural response to stimulants in children is similar regardless of whether they have ADHD or not.

Stimulant medication is an effective treatment for Adult Attention-deficit hyperactivity disorder although the response rate may be lower for adults than children. Some physicians may recommend antidepressant drugs as the first line treatment instead of stimulants although antidepressants have lower treatment effect sizes than stimulant medication.

A study shown that children taking stimulant medications tend to be lighter in weight and shorter than their peers.

## Amphetamine based medications

Three different medicines derived from amphetamine are used in ADHD treatment. Their trade names are Adderall (a mixture of 72% dextroamphetamine and 28% levoamphetamine), Dexedrine (pure dextroamphetamine), and Desoxyn (pure dextromethamphetamine). The differences in these three Amphetamine based medications' active compounds and mixture ratios results in each medications' slightly different activities.

### *Levoamphetamine and dextroamphetamine*

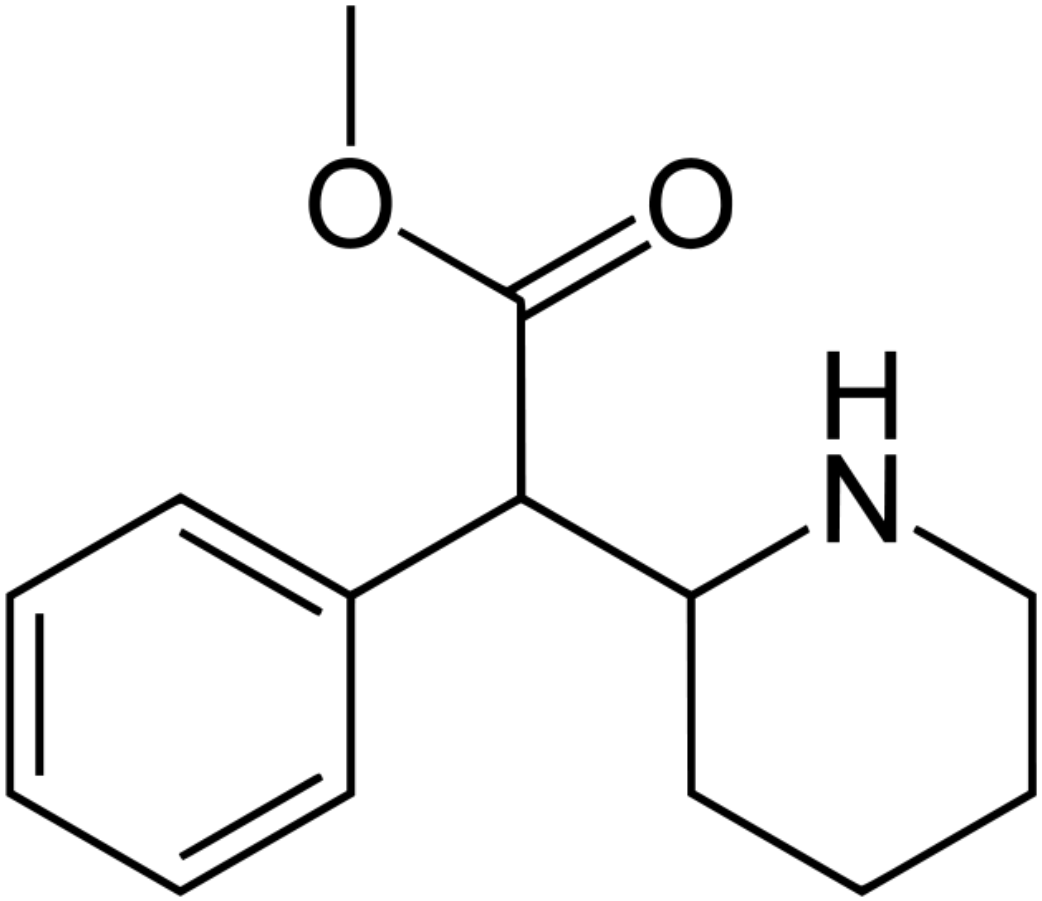
Levoamphetamine and dextroamphetamine have the same chemical formula but are mirror images of each other, the same way that a person's hands are the same but are mirror images of each other. This mirror difference is enough to cause the two compounds to be metabolized differently. Adderall begins to work before dextroamphetamine because of levoamphetamine. Levoamphetamine also provides Adderall with a longer clinical effect than dextroamphetamine. However, the brain’s preference for dextroamphetamine over levoamphetamine shows that the clinical value of Adderall is, for the most part, due to dextroamphetamine. A few children with ADHD and comorbid disorders have helpful responses to levoamphetamine.

### *Dextromethamphetamine*

The body metabolizes dextromethamphetamine into dextroamphetamine (in addition to less important chemicals). A quarter of dextromethamphetamine will ultimately become dextroamphetamine. After comparing only the common ground between dextroamphetamine and dextromethamphetamine, the latter is said to be the stronger stimulant. In theory—and in practice—a larger dose of dextroamphetamine is needed to achieve dextromethamphetamine’s clinical potency. In fact, when dextroamphetamine and methylphenidate are unhelpful, some doctors may prescribe dextromethamphetamine. Although more rarely prescribed, anecdotal reports suggest

dextromethamphetamine is very helpful in cases where the other two are ineffective, or cause limiting side effects.

## Methylphenidate based medications




Methylphenidate

There are two different medicines derived from methylphenidate: Ritalin, which is half dextrothreomethylphenidate and half levothreomethylphenidate, and Focalin, which is pure dextrothreomethylphenidate. Dextrothreomethylphenidate has a higher pharmacological activity than its mirror *levo*-form or enantiomer. Levothreomethylphenidate has much weaker activity than the *dextro* isomer, and so for instance if Daytrana (Ritalin in transdermal patch form) is used, then the levothreomethylphenidate comprising half of the administered dose, accounts for only around one thirteenth of the total clinical effect.

## Controlled release of drugs

Doctors may prescribe a controlled release pharmaceutical so that patients only have to take medication in the morning, or at a time more convenient for the patient. This is especially helpful for children who do not like taking their medication in the middle of the school day. Several controlled release methods are used in the U.S. FDA-approved medications for ADHD. Each way provided makes the FDA drugs pharmaceutically different.

### *Multiple beads*

Adderall and Dexedrine Spansules are examples of pharmaceuticals that use a system of two beads to achieve a controlled release. The beads are contained in a gelatin capsule that quickly dissolves in water, thus releasing the beads. The two different types of beads dissolve at different rates, thus extending the effects of the amphetamines. The company that markets Adderall is developing a new version of Adderall with three different kinds of beads that would be effective for up to 16 hours.

### *Osmosis*

The only ADHD medication that currently utilizes osmotic pressure to achieve a controlled release of medicine is Concerta. A tablet of Concerta is actually a coated capsule. The coating is a mix of methylphenidate hydrochloride and binders such as lactose, povidone, and carnauba wax. Under that coating is a hollow filled capsule made of a semipermeable rigid membrane. The actual capsule is insoluble in water, but some of the ingredients that fill the capsule are water-soluble and others react in special ways with water. At one end of the capsule there is a laser drilled small hole, big enough for methylphenidate particles to pass through. The capsule's volume is partitioned into three sections. At the end closest to the hole is the first partition, which is a mixture containing a small concentration of methylphenidate. In the middle is the second partition is a different mixture that contains a higher concentration of methylphenidate. Occupying the third of the capsules volume that is furthest away from the small hole is triacetin, cellulose acetate, hypromellose, polyethylene glycol and polyethylene oxides.

Once swallowed, the capsule's shell quickly disintegrates and the methylphenidate that was contained in the shell is released. When water sweeps through the semipermeable membrane, the third partition that is furthest away from the capsule's hole will grow because the hypromellose absorbs water and swells up and the polyethylene glycol will increase the osmotic pressure. This partition will slowly push the contents of the other two partitions out the small hole, starting with the lower concentrations of methylphenidate, once the lower concentration of methylphenidate has mostly left the capsule the higher concentration of methylphenidate will begin to be pushed out of the capsule's hole. The capsule will be pharmacologically inactive once all the methylphenidate is expelled.

### *Transdermal*

This is a patch applied to the skin that allows the drug to diffuse through the skin layers and enter the bloodstream. Unlike oral drugs, it may be removed and replaced conveniently, so it is flexible around the patient's schedule. Daytrana is the brand name of a transdermal patch which is essentially the same formulation as Ritalin. Daytrana is applied to the skin in the morning and the drug is evenly absorbed throughout the day, the patient should expect to feel the effects of the methylphenidate until two hours after the patch was removed, so patients should expect to take the patch off a few hours before bedtime. The collaborators that developed Daytrana are developing a transdermal patch version of dextroamphetamine and have completed phase I U.S. FDA human studies. This medicinal patch is code named SPD483 (a.k.a., ATS; Amphetamine Transdermal System; Amphetamine patch).

### *Prodrug*

A prodrug is a compound which is itself inactive, but when metabolized becomes pharmacologically active. Prodrugs are usually designed to improve oral bioavailability as the chemical properties of the active compound may cause it to be poorly absorbed from the gastrointestinal tract. Lisdexamfetamine (Sold as Vyvanse) is a prodrug of dextroamphetamine. Vyvanse is a gelatin capsule that quickly dissolves once swallowed releasing lisdexamfetamine dimesylate.

## Non stimulants

Atomoxetine (Strattera) is a non-stimulant drug approved for the treatment of attention-deficit hyperactivity disorder (ADHD). It is less effective than stimulants for ADHD, is associated with individual cases of liver damage, carries a U.S. FDA black box warning regarding suicidal idealization, and controlled studies show increases in heart rate, decreases of body weight, decreased appetite and treatment-emergent nausea.

Certain antidepressants such as tricyclic antidepressants, SNRIs or MAOIs are sometimes prescribed and are also effective in the treatment of ADHD.

## Off-label medications

Some medications used to treat ADHD are prescribed off-label, outside the scope of their FDA-approved indications for various reasons. The U.S. FDA requires numerous clinical trials to prove a potential drug's safety and efficacy in treating ADHD. The drugs below have not been through these tests, so the efficacy is unproven (however these drugs have been licensed for other indications, so have been proven to be safe in those populations), however proper dosage and usage instructions are not as well characterized.

- Amantadine (Symmetrel) — an antiviral drug and dopamine agonist. There have been reports of low-dose amantadine having been successfully used off-label to treat ADHD.

- Amineptine (Survector/Maneon) — a tricyclic antidepressant now illegal in many countries for being thought to have a small potential for abuse. It is still legal in some parts of the EU, such as Spain and Italy; it is no longer available in the U.S., Canada, France or the UK.
- Benzphetamine (Didrex) — a less powerful stimulant. It has little psychoactive effects until the liver metabolizes it into amphetamine and methamphetamine. Since this acts as a sustained release mechanism, it has lower abuse potential and is schedule 3.
- Bupropion (Wellbutrin) is classified as an antidepressant. It is the most common of off-label prescription for ADHD. It inhibits the reuptake of norepinephrine, and to a lesser extent, dopamine, in neuronal synapses, and has little or no effect on serotonergic re-uptake. Bupropion is not a controlled substance. It is commonly prescribed as a timed release formulation to decrease the risk of side effects. Bupropion is not particularly known for its stimulant properties because at high doses it tends to cause seizures in a large portion of the population.
- Clonidine — Initially developed as a treatment for high blood pressure, low doses in evenings and/or afternoons are sometimes used in conjunction with stimulants to help with sleep and because Clonidine sometimes helps moderate impulsive and oppositional behavior and may reduce tics. It may be more useful for comorbid Tourette syndrome.
- Milnacipran, an anti-depressant drug, is currently being investigated for potential to alleviate the symptoms of ADHD in adults.
- Modafinil (Provigil/Alertec/Sparlon) — In the U.S., it is off-label pending decision by the FDA on August 22, 2006. It was originally pending marketing on-label as Alertec but denied for a reported incidence of Stevens-Johnson Syndrome.
- Pemoline (Cylert) — a stimulant used with great success until the late 1980s when it was discovered that this medication could cause liver damage. In March 2005, the makers of Cylert announced that it would discontinue the medication's production. It is no longer available in the United States.
- Reboxetine (Edronax) — is a selective norepinephrine reuptake inhibitor which is mainly used as an antidepressant. Studies outside the USA have found it to be an effective treatment for ADHD, and it is prescribed off-label for this purpose in Israel and some European countries, however reboxetine has never been approved by the FDA in the United States.
- Selegiline — an MAOI currently being investigated for ADHD.
    - Emsam is a version of Selegiline delivered via transdermal patch.

Tricyclic anti-depressants are also occasionally prescribed, but they seem to only treat the hyperactive part of the condition. There is research on the selective serotonin reuptake enhancer class of medications (SSREs); currently, the only one available is tianeptine (trade name Stablon); this is an atypical tricyclic anti-depressant which is inconclusive in its efficacy and hence not approved. Tianeptine is not available in North America.

## Antipsychotic medication


Risperdal (risperidone) 4 mg tablets

In an odd contrast with the use of stimulant medication approved by the U.S. FDA as a treatment for children with ADHD, the use of atypical antipsychotic drugs as an off-label treatment has been rising. Antipsychotics work by blockingdopamine, whereas stimulants trigger its release. Atypical antipsychotics have been approved for use in children and teenagers with schizophrenia spectrum disorders and autistic spectrum disorders by the U.S. FDA) since 1993.

Non-ADHD children do not respond differently to ADHD children when prescribed antipsychotic drugs, which are also increasingly prescribed off-label for children with aggression or defiant behavior. Social pressure to control a child's difficult and disruptive behavior, both at home and at school, may inadvertently change focus from what is in the best interest of the child's wellbeing; to how to render the child more compliant and easier to manage.

Careful approach needs to be taken when blocking dopamine function, which is responsible for the psychological reward system. Excessive blocking of this neurotransmitter can causedysphoria. This may in turn cause suicidal ideation, or lead some teenagers to compensate for their dopamine deficiency with illicit drugs or alcohol. Atypical antipsychotics are preferred for this reason, because they are less likely to cause movement disorders, dysphoria, and increased drug cravings that have been associated with older typical antipsychotics.Weight gain, diabetes, lactation, gynecomastia, drooling, dysphoria, anhedonia (inability to experience pleasure), fatigue, sexual dysfunction, heart rhythm problems and the possibility of tardive dyskinesia, an irreversible movement disorder, are among the adverse events associated with antipsychotic drugs.

## Other non-stimulant medications

Atomoxetine (Strattera) and Guanfacine (Intuniv) are the only non-stimulant drugs approved for the treatment of ADHD. Other medications which may be prescribed off-label include $\alpha_{2A}$ adrenergic receptor agonists such as clonidine, certain antidepressants such as tricyclic antidepressants, SNRIs, SSRIs or MAOIs.

## *Experimental and alternative medicine*

Ginkgo is a natural supplement used by some with ADHD

Dietary supplements and specialized diets are sometimes used by people with ADHD with the intent to mitigate some or all of the symptoms. For example, Omega-3 supplementation (seal, fish or krill oil) may reduce ADHD symptoms for a subgroup of children and adolescents with ADHD "characterized by inattention and associated neurodevelopmental disorders." Although vitamin or mineral supplements (micronutrients) may help children diagnosed with particular deficiencies, there is no evidence that they are helpful for all children with ADHD. Furthermore, *megadoses of vitamins, which can be toxic, must be avoided.* In the United States, no dietary supplement has been approved for the treatment for ADHD by the FDA. There is however a pilot study done which shows that phosphatidyl serine (PS) can help against ADHD.

Some people report short-term positive results using medical cannabis for treating ADHD and doctor David Bearman supported this treatment. However, long-term effects of cannabis use include substance dependence, drug tolerance, increase risk for schizophrenia, bipolar disorders, and major depression.

EEG biofeedback is a treatment strategy used for children, adolescents and adults with ADHD. The human brain emits electrical energy which is measured with electrodes on the brain. Biofeedback alerts the patient when beta waves are present. This theory believes that those with ADHD can train themselves to decrease ADHD symptoms. There is a distinct split in the scientific community about the effectiveness of the treatment. A number of studies indicate the scientific evidence has been increasing in recent years for the effectiveness of EEG biofeedback for the treatment of ADHD. According to a 2007 review, with effectiveness of the treatment was demonstrated to be equivalent to that of stimulant medication. The review noted, improvements are seen at the behavioral and neuropsychological level with the symptoms of inattention, hyperactivity and impulsivity showing significant decreases after treatment. There are no known side effects from EEG biofeedback therapy. There are methodological limitations and weaknesses in study designs however. In a 2005 review, Loo and Barkley stated that problems including lack of blinding such as placebo control and randomisation are significant limitations to the studies into EEG biofeedback and make definitive conclusions impossible to make. As a result more robust clinical studies have been strongly recommended. A German review in 2004 found that EEG biofeedback, also sometimes referred to as neurofeedback, is more effective than previously thought in treating attention deficiency, impulsivity and hyperactivity; short-term effects match those of stimulant treatment and a persistent normalization of EEG parameters is found which is not found after treatment with stimulants. There are no known side effects from biofeedback therapy although research into biofeedback has been limited and further research has been recommended. An American review the following year also emphasized the benefits of this method. Similar findings were reported in a study by another German team in 2004.

Aerobic fitness may improve cognitive functioning and neural organization related to executive control during pre-adolescent development, though more studies are needed in

this area. One study suggests that athletic performance in boys with ADHD may increase peer acceptance when accompanied by fewer negative behaviors.

Art is thought by some to be an effective therapy for some of the symptoms of ADHD. Other sources, including some psychologists who have written on the subject, feel that cutting down on time spent on television, video games, or violent media can help some children. One study indicated a correlation between excessive TV time as a child with higher rates of ADHD symptoms. Other therapies that have been effective for some have been ADHD coaching, positive changes in diet, such as low sugar, low additives, and no caffeine. Children who spend time outdoors in natural settings, such as parks, seem to display fewer symptoms of ADHD, which has been dubbed "Green Therapy". Alternative therapies are often sought out due to concerns of the long-term effects of stimulants on children. Parents, children, consumer advocacy organizations and some physicians are increasingly looking for alternatives to stimulant drugs. There is a large body of evidence of effectiveness of some alternative therapies including supplementation with certain nutrients, elimination diets, avoidance of food additives or dyes, allergy treatment, family counseling and behavior therapy. Some advocate that alternative therapies should be tried before ADHD medications although not all ADHD children will have an effective response.

## Aerobic fitness

Aerobic fitness may improve cognitive functioning and neural organization related to executive control during pre-adolescent development, though more studies are needed in this area. One study suggests that athletic performance in boys with ADHD may increase peer acceptance when accompanied by fewer negative behaviors.

## Biofeedback

EEG biofeedback, also sometimes referred to as neurofeedback, is effective in treating attention, impulsivity and hyperactivity. There are no known side effects from biofeedback therapy although research into biofeedback has been limited and further research has been recommended. One 2009 study concluded "that NF may be considered as a clinically effective module in the treatment of children with ADHD"

## Dietary supplements

There are indications that children with ADHD are metabolically different from others.

- Zinc- Although the role of zinc in ADHD has not be elucidated, "numerous controlled studies report cross-sectional evidence of lower zinc tissue levels."
- Omega-3 fatty acids - Some studies suggest that a lack of omega-3 fatty acids is associated with certain ADHD symptoms. and it has therefore been suggested that diet modification may play a role in the management of ADHD. People with ADHD were found to have significantly lower plasma phospholipids and erythrocytes omega-3 fatty acids. Their intake of saturated fat was found to be

30% higher than in controls, while the intake of many other nutrients was not different. In support of the idea that it is not the intake of essential fatty acids that causes low tissue levels, a preliminary study showed that exhaled ethane, a marker of omega-3 fatty acids peroxidation, was higher in children with ADHD relative to controls. Researchers from CSIRO, Australia's national science agency, showed polyunsaturated fatty acids to provide "medium to strong positive treatment effects" in ADHD. Another double blind study conducted by the University of Oxford, where children were given omega 3 fatty acids concluded that "significant improvements for active treatment versus placebo were found in reading, spelling, and behavior over 3 months of treatment in parallel groups." A 2008 study also concludes that Omega-3/Omega-6 supplementation reduces ADHD-symptoms for some. Thus it increasingly is documented in clinical studies that omega 3 fatty acids provide a safe way to treat hyperactivity.

- Magnesium and vitamin $B_6$ (pyridoxine) - In 2006, a study demonstrated that children with autism had significantly lower magnesium than controls, and that the correction of this deficit was therapeutic: Mousain-Bosc *et al.* showed that children with ADHD (n =46) had significantly lower red blood cell magnesium levels than controls (n =30). Intervention with magnesium and vitamin $B_6$ reduced hyperactivity, hyperemotivity/aggressiveness and improved school attention.
- Iron supplements - In 2005, the official journal of the American Academy of Pediatrics, Pediatrics, published the case report of a child with ADHD with low ferritin who showed "considerable behavioral improvement" after his ferritin was normalized by iron supplementation. Based on earlier studies on iron deficiency and attentional function (notably the dopamine synthesis aspect), the screening of ferritin levels in children with ADHD was suggested.
- Potassium - In 2007, Harvard-associated researchers described a form of ADHD that was well treated with over-the-counter potassium supplements. The molecular mechanism suggested by the authors was one producing sensory overstimulation, often triggered by ingesting carbohydrates, suggesting that people with ADHD who have sensitivity to sugar may be particularly likely to have this variant.
- In the 1980s vitamin $B_6$ was promoted as a helpful remedy for children with learning difficulties including inattentiveness; however, a study of large doses of vitamins with ADHD children showed that they were ineffective in changing behavior.
- Mild stimulants such as caffeine, theobromine, and nicotine may improve the function of some children suffering from ADHD.

## Diets

Perhaps the best known of the dietary alternatives is the Feingold diet which involves removing salicylates, artificial colors and flavors, and certain synthetic preservatives from children's diets. However, studies have shown little if any effect of the Feingold diet on the behavior of children with ADHD.

A meta-analysis has found that dietary elimination of artificial food coloring and preservatives provides a statistically significant benefit in children with ADHD. Other more recent studies agree with these conclusions. The UK Food Standards Agency (FSA) has called for a ban on the use of six artificial food colorings and the European Union (EU) has ruled that some food dyes must be labeled with the relevant E number as well as this warning: *"may have an adverse effect on activity and attention in children."*

## *Comorbid disorders*

Because ADHD comorbidities are diverse and the rate of comorbidity is high, special care must dedicated to certain comorbidities. The FDA is not set up to address this issue, and does not approve medications for comorbidities, nonetheless certain such topics have been extensively researched.

### Tic disorders

Patients with Tourette syndrome who are referred to specialty clinics have a high rate of comorbid ADHD. Patients who have ADHD along with tics or tic disorders may also have problems with disruptive behaviors, overall functioning, and cognitive function, accounted for by the comorbid ADHD.

The treatment of ADHD in the presence of tic disorders has long been a controversial topic. Past medical practice held that stimulants (such as Ritalin) could not be used in the presence of tics, due to concern that their use might worsen tics; however, multiple lines of research have shown that stimulants can be cautiously used in the presence of tic disorders. Several studies have shown that stimulants do not exacerbate tics any more than placebo does, and suggest that stimulants may even reduce tic severity. Controversy remains, and the PDR continues to carry a warning that stimulants should not be used in the presence of tic disorders, so physicians may be reluctant to use them. Others are comfortable using them and even advocate for a stimulant trial when ADHD co-occurs with tics, because the symptoms of ADHD can be more impairing than tics.

The stimulants are the first line of treatment for ADHD, with proven efficacy, but they do fail in up to 20% of cases, even in patients without tic disorders. Current prescribed stimulant medications include: methylphenidate (brand names Ritalin, Metadate, Concerta), dextroamphetamine (Dexedrine), and mixed amphetamine salts (Adderall). Other medications can be used when stimulants are not an option. These include the alpha-2 agonists (clonidine and guanfacine), tricyclic antidepressants (desipramine and nortriptyline), and newer antidepressants (bupropion and venlafaxine. There have been case reports of tics worsening with bupropion (brand name Wellbutrin). There is good empirical evidence for short-term safety and efficacy for the use of desipramine, bupropion and atomoxetine (Strattera).

## *Concerns about stimulant medication*

The National Institute of Mental Health states that, "stimulant drugs, when used with medical supervision, are usually considered quite safe." Still, some parents and professionals have raised questions about the side effects of drugs and their long term use. A recent review states that ADHD studies "have major methodological deficiencies which are compounded by their restriction to school-age children, relatively short follow-up, and few data on adverse effects."

The American Heart Association feel that it is prudent to carefully assess children for heart conditions before treating them with stimulant medications.

### Increase in use

Outpatient treatment rates have held steady in the US recently. Prior to this, outpatient treatment for ADHD in the US grew from 0.9 children per 100 in 1987 to 3.4 per 100 in 1997. There is concern about the rising use of methylphenidate (Ritalin), mainly to treat ADHD and similar disorders, in the UK. The incidence of ADHD is estimated at three to five percent of the population, while the number of children in the United States taking Ritalin is estimated at one to two percent. In a small study of four American communities, the reported incidence of ADHD varied from 1.6% to 9.4%. The study also found that only 12.5% of the children reportedly meeting the DSM-III-R ADHD criteria for ADHD had been treated with stimulants during the past year.

### Stimulant misuse

There is non-medical prescription stimulant use. A 2003 study found that non prescription use by college students in the US was 6.9% with 4.1% using them within the last year. A 2006 study with teens in Grades 7 to Grade 12 found that 2% reported non-medical use of prescription stimulant medication in the past 12 months, with 2% also reporting non-medical use of prescribed sedatives/and or anxiety medications, 3% using sleeping medications, and 12% reporting non-medical use of prescribed pain medications.

### Medication in preschoolers

It is believed that ADHD affects seven percent of the preschool-aged population. Michael J. Manos of the Cleveland hospital for Children states, "Severe ADHD in children 2–4 years of age is especially problematic. Young children do not have the ability to use or respond to language to moderate behavior that older children have." Evidence indicates that forty percent of children who show signs of ADHD are suspended from preschool, while approximately sixteen percent are eventually expelled. The disorder, which makes it difficult for children to control their behavior and pay attention, affects about 7 percent of the school-aged population. Parents of children with ADHD note that they usually display their symptoms at an early age. Dr. John Van Brakle has stated, "pediatricians have long questioned whether such children can accurately be identified, given the overlap with normal behaviors in young children." The use of stimulant medication has

not been approved by the FDA for children under the age of six. A growing trend is the diagnosis of younger children with ADHD. Prescriptions for children under the age of 5 rose nearly 50 percent from 2000 to 2003. Research on this issue has indicated that stimulant medication can help younger children with "severe ADHD symptoms" but typically at a lower dose then older children. It was also found that children at this age are more sensitive to side effects and should be closely monitored. Manos states, "it is prudent for physicians to be cautious," with medications. Evidence suggests that careful assessment and highly individualized behavioural interventions significantly improve both social and academic skills while medication only treats the symptoms of the disorder. Manos suggests that, "one of the primary reasons cited for the growing use of psychotropic interventions was that many physicians realize that psychological interventions are costly and difficult to sustain."

A study published in the November 2006 *Journal of the American Academy of Child and Adolescent Psychiatry* followed 300 three- to five-year-olds with severe ADHD (hyperactive/impulsive, inattentive, or combined type). One-third of those children experienced reduced ADHD symptoms after engaging in 10 weeks of behavior modification techniques wherein parents offered consistent praise, ignored negative behavior, and used time-outs. The remaining two-thirds showed improvement with a combination of behavior therapy and low doses of Ritalin. 11% of the children stopped treatment due to side effects including appetite reduction, insomnia, and anxiety.

## Adverse effects

A number of possible side effects are of concern with respect to ADHD medications.

### Tics

The emergence or worsening of tics have been thought to occur. Despite belief to the contrary, no significant effects have been observed on the emergence of tics.

### Growth Delay and Weight Loss

The stunting of growth in children has been a concern. Past studies suggested that "long-term use of the drugs could stunt children's growth." However, more recent studies suggest that children eventually do reach normal height and weight. According to Wilens (2004), treated children with ADHD tend to grow at a slower rate but catch up during adolescence and adulthood. One notion is that psychostimulant medication can decrease appetite which may result in loss of weight and may be a factor in stunted growth.

### Cardiovascular side effects

There is concern that stimulants and Atomoxetine, which increase the heart rate and blood pressure, might cause serious cardiovascular problems.

In 2007 the FDA requires all ADHD drug manufacturers to notify patients about serious cardiovascular side effects. This was due to reports of sudden death in children taking these medications who had underlying heart problems and of high risk adults who suffered heart attacks and strokes.

Studies indicated that, "the rate of sudden death of children taking ADHD medications do not appear to exceed the base rate of sudden death in the general population". Matthew Smith is purported to have died at age 14 after long-term use of Ritalin. The medical examiner determined that Smith died from Ritalin usage, but medical experts dispute this. The examiner also argued that it was likely that diabetic children were at higher risk for cardiac problems.

## Psychiatric side effects

In 2006 the FDA examined the occurrence of psychiatric side effects in ADHD medication. They found increased rates of psychosis and or mania with all drug treatments examined, including: Concerta, Ritalin LA, d-MPH, Atomoxetine, Adderall XR, Modafinil, MTS, and Metadate.

Sleep problems may occur.

Many of these drugs are associated with physical and psychological dependence.

### Issues with long-term use of stimulant medication

The short term use of stimulant medication has been shown to be effective yet its long term effects are yet to be determined. The Multimodal Treatment Study of Children with ADHD study concluded that while drugs such as Ritalin and Concerta (a delayed release form of Ritalin) worked in the short term, there was no demonstrable improvement in children's behavior after three years of medication."

Wilens and other professionals have shown that the controlled use of medication can reduce the likelihood of substance abuse later on. Biederman and colleagues reported on a longitudinal study in which it was found that unmedicated children with ADHD were at greater risk of later substance use. Children who received medication for their ADHD were less likely to later use substances. A 2007 study from the Mayo clinic found that, "treatment with stimulant medication during childhood was associated with more favorable long-term school outcomes."

### Long term use and schizophrenia and drug induced psychosis

Although the safety profile of short-term methylphenidate therapy in clinical trials has been well established, repeated use of psychostimulants such as methylphenidate is less clear. The long term effects of methylphenidate in drug addiction, withdrawal reactions, psychosis, depression, and pregnancy has received very little research and thus the long term effects of using stimulants for ADHD are largely unknown. There are no well

defined withdrawal schedules for discontinuing long term use of stimulants. Short term clinical trials have shown an incidence of psychosis of 0.1%. Psychosis occurs more commonly as a result of chronic use effecting about 6% of children on long term methylphenidate. The long term effects on mental health disorders in later life of chronic use of methylphenidate is unknown. Concerns have been raised that long-term therapy might cause drug dependence, paranoia, schizophrenia and behavioral sensitisation, similar to other stimulants. Psychotic symptoms from methylphenidate can include, hearing voices, visual hallucinations, urges to harm oneself, severe anxiety, euphoria, grandiosity, paranoid delusions, confusion, increased aggression and irritability. Methylphenidate psychosis is unpredictable in who it will occur. Family history of mental illness does not predict the incidence of stimulant toxicosis in ADHD children. High rates of childhood stimulant use are found in ADHD patients who will eventually be diagnosed with comorbid schizophrenia and bipolar disorder. Individuals with a diagnosis of bipolar or schizophrenia who were prescribed stimulants during childhood typically have a significantly earlier onset of the psychotic disorder and suffer a more severe clinical course of psychotic disorder.

## Stimulant withdrawal and rebound effects

Stimulant withdrawal or rebound reactions can occur and should be minimised in intensity, i.e. via a gradual tapering off of medication over a period of weeks or months. A very small study of abrupt withdrawal of stimulants did suggest that withdrawal reactions are not typical. Nonetheless withdrawal reactions may still occur in susceptible individuals. The withdrawal or rebound symptoms of methylphenidate can include psychosis, irritability and depression and a return of ADHD symptoms in an exaggerated form. Methylphenidate may be worse for causing rebound and withdrawal effects due to its very short half life. Amphetamine may cause less severe rebound or withdrawal effects due to its somewhat longer half life. Up to a third of ADHD children experience a rebound effect in ADHD symptoms when the methylphenidate dose wears off.

## Cancer

A small-scale 2005 Texas study indicated that methylphenidate might cause chromosome aberrations. At the time this study caused concern because of the link between chromosome aberrations and cancer. The authors of the study stated that all the children in this study showed suspicious DNA changes within a very short time and suggested that further research was warranted. A team from the Food and Drug Administration (FDA), the National Institutes of Health (NIH) and the Environmental Protection Agency (EPA) went to Texas in 2005 to evaluate the methodology of the study. Dr. David Jacobson-Kram of the FDA said that the study had flaws in its methods but that its results could not be dismissed. Flaws cited are (1) that the study did not include a control group on placebo, and (2) that it is too small. A follow up study led by a team of six scientists from the Department of Child and Adolescent Psychiatry and Psychotherapy and the Department of Toxicology, University of Würzburg, Würzburg, Germany looked at this issue with an in-depth study. They sought to respond to the challenge noted above to attempt to replicate the results of El-Zein et al. in a larger study. Their paper was

completed in 2006 and published in 2007 in Environmental Health Perspectives (EHP), the peer-reviewed journal of the United States' National Institute of Environmental Health Sciences. This study used a larger cohort and a longer period of follow-up and included a small group of long-term users, but otherwise used what researchers believed to be an identical methodology to that used by El-Zein et al. (They note that El-Zein et al. published a short study report and did not publish detailed descriptions of methodology.) After follow-ups at six months, the researchers found no evidence that methylphenidate might cause cancer, stating "the concern regarding a potential increase in the risk of developing cancer later in life after long-term MPH treatment is not supported."

## *Cost effectiveness*

Combined medical management and behavioral treatment is the most effective ADHD management strategy, followed by medication alone, and then behavioral treatment. In terms of cost-effectiveness, management with medication has been shown to be the most cost-effective, followed by behavioral treatment, and combined treatment. The individually most effective and cost efficient way is with stimulant medication. Additionally, long-acting medications for ADHD, in comparison to short-acting varieties, generally seem to be cost effective. Comorbid (relating to two diseases that occur together, e.g. depression and ADHD) disorders make finding the right treatment and diagnosis much more costly than when comorbid disorders are absent.

## *History*

The first reported evidence of stimulant medication used to treat children with concentration and hyperactivity problems came in 1937. Dr. Charles Bradley in Providence, Rhode Island reported that a group of children with behavioral problems improved after being treated with the stimulant Benzedrine. In 1957, the stimulant methylphenidate (Ritalin, which was first produced in 1950) became available under various names (including Focalin, Concerta, Metadate, and Methylin); it remains one of the most widely prescribed medications for ADHD. Initially the drug was used to treat narcolepsy, chronic fatigue, depression, and to counter the sedating effects of other medications. The drug began to be used for ADHD in the 1960s and steadily rose in use.

In 1975, pemoline (Cylert) was approved by the U.S. FDA for use in the treatment of ADHD. While an effective agent for managing the symptoms, the development of liver failure in 14 cases over the next 27 years would result in the manufacturer withdrawing this medication from the market. New delivery systems for medications were invented in 1999 that eliminated the need for multiple doses across the day or taking medication at school. These new systems include pellets of medication coated with various time-release substances to permit medications to dissolve hourly across an 8–12 hour period (Metadate CD, Adderall XR, Focalin XR) and an osmotic pump that extrudes a liquid methylphenidate sludge across an 8–12 hour period after ingestion (Concerta).

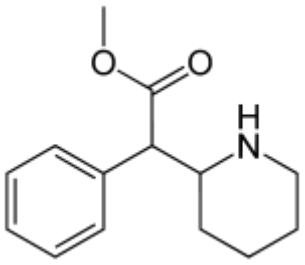
In 2003, atomoxetine (Strattera) received the first FDA approval for a nonstimulant drug to be used specifically for ADHD. In 2007, lisdexamfetamine (Vyvanse) becomes the first prodrug to receive FDA approval for ADHD.

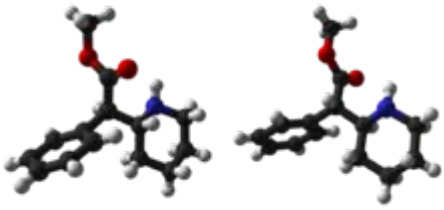
In 1999 the largest study of treatment for ADHD was published in the *American Journal of Psychiatry*. Known as the *Multimodal Treatment Study of ADHD* (MTA Study), it involved more than 570 children with ADHD at 6 sites in the United States and Canada randomly assigned to 4 treatment groups. All 4 treatment groups showed marked improvement from the time of baseline measurements to completion of the study 14 months later. Behavioral treatment was as effective as medication alone on 16 of 19 outcome measures. This was especially good for the behavior modification group, since the behavioral protocols were faded 3 months prior to the last evaluation and the stimulant group continued to receive medication right up to the last evaluation point.

# Chapter 19

# Methylphenidate

**Methylphenidate**



| Systematic (IUPAC) name | |
|---|---|
| methyl phenyl(piperidin-2-yl)acetate | |
| **Identifiers** | |
| **CAS number** | 113-45-1 |
| **ATC code** | N06BA04 |
| **PubChem** | CID 4158 |
| **DrugBank** | DB00422 |
| **ChemSpider** | 4015 ✓ |
| **UNII** | 207ZZ9QZ49 ✓ |
| **KEGG** | D04999 ✓ |
| **ChEMBL** | CHEMBL796 ✓ |
| **Chemical data** | |

| | |
|---|---|
| **Formula** | $C_{14}H_{19}NO_2$ |
| **Mol. mass** | 233.31 g/mol |
| **SMILES** | eMolecules & PubChem |
| **Physical data** | |
| **Melt. point** | 214 °C (417 °F) |
| **Pharmacokinetic data** | |
| **Bioavailability** | 11–52% |
| **Protein binding** | 30% |
| **Metabolism** | Liver (80%) |
| **Half-life** | 2–4 hours |
| **Excretion** | Urine |
| **Therapeutic considerations** | |
| **Licence data** | US FDA:link |
| **Pregnancy cat.** | C |
| **Legal status** | Controlled (S8) (AU) Schedule III (CA) POM (UK) Schedule II (US) |
| **Routes** | Oral, Sublingual, Transdermal, IV, Nasal |

**Methylphenidate** (**MPH**; **Ritalin**, **Concerta**, **Metadate**, or **Methylin**) is a psychostimulant drug approved for treatment of attention-deficit hyperactivity disorder, postural orthostatic tachycardia syndrome, and narcolepsy. It may also be prescribed for off-label use in treatment-resistant cases of lethargy, depression, neural insult, obesity, and rarely other psychiatric disorders such as obsessive-compulsive disorder.

Methylphenidate belongs to the piperidine class of compounds and increases the levels of dopamine and norepinephrine in the brain through reuptake inhibition of the monoamine transporters. It also increases the release of dopamine and norepinephrine. MPH possesses structural similarities to amphetamine, and, though it is less potent, its pharmacological effects are even more closely related to those of cocaine.

MPH is most commonly known by the Novartis trademark name **Ritalin**, which is an instant-release racemic mixture, although a variety of formulations and generic brand names exist. Other brand names include **Ritalina**, **Rilatine**, **Attenta**, **Methylin**, **Penid**, and **Rubifen**; and the sustained release tablets **Concerta**, **Metadate CD**, **Methylin ER**, **Ritalin LA**, and **Ritalin-SR**. **Focalin** is a preparation containing only dextro-methylphenidate, rather than the usual racemic dextro- and levo-methylphenidate mixture

of other formulations. A newer way of taking methylphenidate is by using a transdermal patch (under the brand name **Daytrana**), similar to those used for nicotine replacement therapy.

## *History*

Methylphenidate was first synthesized in 1944, and was identified as a stimulant in 1954.

Methylphenidate was synthesized by Ciba chemist Leandro Panizzon. His wife, Marguerite, had low blood pressure and would take the drug as a stimulant before playing tennis. He named the substance Ritaline, after his wife's nickname, Rita.

Originally it was marketed as a mixture of two racemates, 80% (±)-erythro and 20% (±)-threo. Subsequent studies of the racemates showed that the central stimulant activity is associated with the threo racemate and were focused on the separation and interconversion of the erythro isomer into the more active threo isomer.

Beginning in the 1960s, it was used to treat children with ADHD or ADD, known at the time as hyperactivity or minimal brain dysfunction (MBD). Production and prescription of methylphenidate rose significantly in the 1990s, especially in the United States, as the ADHD diagnosis came to be better understood and more generally accepted within the medical and mental health communities.

Most brand-name Ritalin is produced in the United States, and methylphenidate is produced in the United States, Mexico, Argentina, Spain and Pakistan. Other generic forms, including "Methylin", "Metadate" and "Attenta" are produced by numerous pharmaceutical companies throughout the world. Ritalin is also sold in Canada, Australia, the United Kingdom, Spain, Germany and other European countries (although in much lower volumes than in the United States). In Belgium the product is sold under the name "Rilatine" and in Brazil and Portugal as "Ritalina".

Sustained-release preparations of methylphenidate are now also available. These include various preparations (e.g. "Ritalin LA", "Equasym XL") that provide two standard doses - half the total dose being released immediately and the other half released four hours later - providing approximately eight hours of continuously sustained effect. In 2000 Janssen received U.S. Food and Drug Administration (FDA) approval to market "Concerta", a controlled-release methylphenidate tablet providing a continuous effect for up to about 12 hours.

## *Mechanism*

According to research of U.S. Department of Energy's Brookhaven National Laboratory methylphenidate works in the treatment of attention deficit hyperactivity disorder by increasing levels of dopamine in the brain. Dopamine, a neurotransmitter, plays a role in feelings of pleasure and is naturally released in rewarding experiences. Neuroimaging studies of medication-free depressed patients have found that depressed subjects have a

functional deficiency of synaptic dopamine. Dopamine decreases "background firing" rates and increases the signal to noise ratio in target neurons by increasing dopamine levels in the brain. As a result, the drug may improve attention and decrease distractibility in activities that normally do not hold the attention of children with attention deficit hyperactivity disorder. However, sympathomimetic amines do have a dependence liability and a potential for tolerance adaptation because of their dopaminergic effects when taken in doses outside of their therapeutic range or for an extended period of time.

## *Therapeutic uses*


Ritalin Uno controlled release capsules (DN)

MPH is the most commonly prescribed psychostimulant and works by increasing the activity of the central nervous system. It produces such effects as increasing or maintaining alertness, combating fatigue, and improving attention. The benefits and cost effectiveness of methylphenidate long term are unknown due to a lack of research. The long term effects of methylphenidate on the developing brain are unknown. Methylphenidate is not approved for children under six years of age.

### Attention deficit hyperactivity disorder

Methylphenidate is approved by the U.S. Food and Drug Administration (FDA) for the treatment of attention-deficit hyperactivity disorder The addition of behavioural modification therapy (e.g. cognitive behavioral therapy (CBT)) has additional benefits on treatment outcome. There is a lack of evidence of the effectiveness in the long term of beneficial effects of methylphenidate with regard to learning and academic performance. A meta analysis of the literature concluded that methylphenidate quickly and effectively reduces the signs and symptoms of ADHD in children under the age of 18 in the short term but found that this conclusion may be biased due to the high number of low quality clinical trials in the literature. There have been no placebo controlled trials investigating

the long term effectiveness of methylphenidate beyond 4 weeks thus the long term effectiveness of methylphenidate has not been scientifically demonstrated. Serious concerns of publication bias regarding the use of methylphenidate for ADHD has also been noted. A diagnosis of ADHD must be confirmed and the benefits and risks and proper use of stimulants as well as alternative treatments should be discussed with the parent before stimulants are prescribed. The dosage used can vary quite significantly from individual child to individual child with some children responding to quite low doses whereas other children require the higher dose range. The dose, therefore, should be titrated to an optimal level that achieves therapeutic benefit and minimal side-effects. This can range from anywhere between 5 mg twice daily to 60 mg four times a day. Therapy with methylphenidate should not be indefinite. Weaning off periods to assess symptoms are recommended.

## Narcolepsy

Narcolepsy, a chronic sleep disorder characterized by overwhelming daytime drowsiness and sudden attacks of sleep, is treated primarily with stimulants. Methylphenidate is considered effective in increasing wakefulness, vigilance, and performance. Methylphenidate improves measures of somnolence on standardized tests, such as the Multiple Sleep Latency Test, but performance does not improve to levels comparable to healthy controls.

## Adjunctive

Use of stimulants such as methylphenidate in cases of refractory depression is controversial. In individuals with cancer, methylphenidate is commonly used to counteract opioid-induced somnolence, to increase the analgesic effects of opioids, to treat depression, and to improve cognitive function. Methylphenidate may be used in addition to an antidepressant for treatment-refractory major depressive disorder. It can also improve depression in several groups including stroke, cancer, and HIV-positive patients. However, benefits tend to be only partial with stimulants being, in general, less effective than traditional antidepressants and there is some suggestive evidence of a risk of habituation. Stimulants may however, have fewer side-effects than tricyclic antidepressants in the elderly and medically ill. A review of the literature found that methylphenidate was ineffective for refractory cases of major depression.

## Substance dependence

Methylphenidate has shown some benefits as a replacement therapy for individuals dependent on methamphetamine. Cocaine and methamphetamine interfere with the protein DAT, over time causing DAT upregulation and lower cytoplasmic dopamine levels in their absence. Methylphenidate and amphetamine have been investigated as a chemical replacement for the treatment of cocaine dependence in the same way that methadone is used as a replacement for heroin. Its effectiveness in treatment of cocaine or other psychostimulant dependence has not been proven and further research is needed.

Early research began in 2007–2008 in some countries on the effectiveness of methylphenidate as a substitute agent in refractory cases of cocaine dependence, owing to methylphenidate's longer half life, and reduced vasoconstricive effects. This replacement therapy is used in other classes of drugs such as opiates for maintenance and gradual withdrawal such as methadone, suboxone, etc.

## Pervasive developmental disorders

Given the high comorbidity between ADHD and autism, a few studies have examined the efficacy and effectiveness of methylphenidate in the treatment of autism. However, most of these studies examined the effects of methylphenidate on attention and hyperactivity symptoms among children with autism spectrum disorders. Aman and Langworthy (2000) attempted to examine the effects of methylphenidate on social-communication and self-regulation behaviors among children with ASDs.

The sample included 33 children with pervasive developmental disorder (29 boys) with a mean age of 6.93 years (range 5–13). This was a 4-week randomized, double-blind, cross-over placebo study, with treatment changing each week between 4 conditions: placebo, low dose, medium dose, and high dose. In this design, neither the experimenters nor the families know which of the 4 treatments the child is receiving at any given time. In addition, the treatment condition changes randomly each week, without anyone knowing the nature of the old or new condition. This allows the experimenters to assume that consistent changes in behaviors that occur during a particular treatment is truly due to the effect of that treatment and not to the expectation of the treatment (placebo effect).

The results indicate that children showed significantly more joint attention behaviors when receiving methylphenidate than when receiving the placebo (although the most effective dosage varied by individual). Furthermore, at a group level, the low dose of methylphenidate resulted in significantly improved joint attention behaviors when compared to the placebo, but no differences were noted between the low, medium, and high doses. Low and medium doses of methylphenidate also resulted in improved self-regulation behavior when compared to placebo.

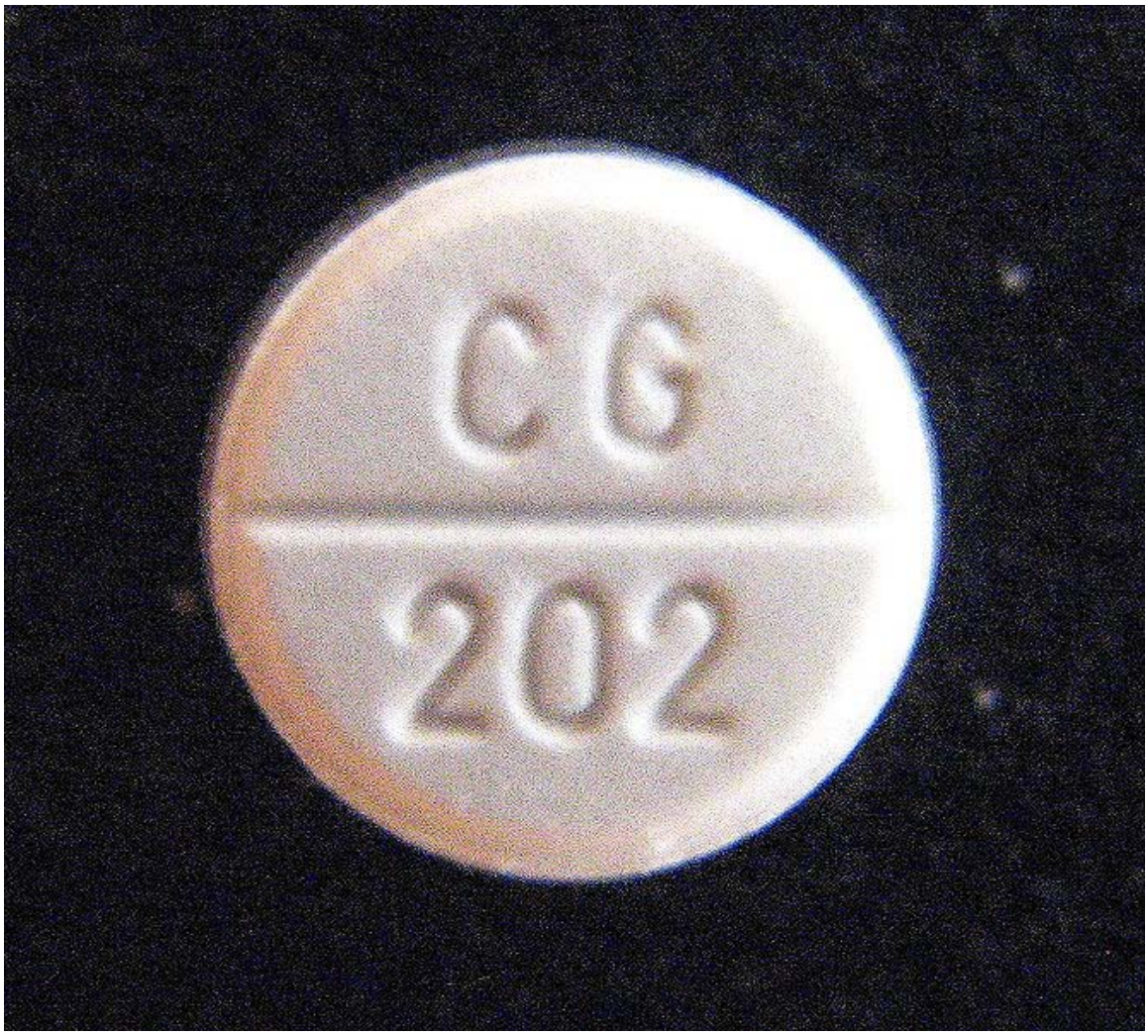
The study presents compelling preliminary evidence suggesting that methylphenidate is effective in improving some social behaviors among children with autism spectrum disorders.

## Investigational

Animal studies using rats with ADHD-like behaviours were used to assess the safety of methylphenidate on the developing brain and found that psychomotor impairments, structural and functional parameters of the dopaminergic system were improved with treatment. This animal data suggests that methylphenidate supports brain development and hyperactivity in children diagnosed with ADHD. However, in normal control animals methylphenidate caused long lasting changes to the dopaminergic system suggesting that if a child is misdiagnosed with ADHD they may be at risk of long lasting adverse effects

to brain development. Animal tests found that rats given methylphenidate grew up to be more stressed and emotional. It is unclear due to lack of followup study whether this occurs in ADHD like animals and whether it occurs in humans. However, long lasting benefits of stimulant drugs have not been found in humans.

## *Delivery formulations*




Ritalin 10 mg tablet (Novartis)


Methylphenidate 10 mg tablets (Mallinckrodt)

Methylphenidate is available in oral tablets or capsules, and in trans-dermal patches. Although most manufacturers do not recommend a dose of more than 60 mg/day, for some adults the prescribed dose may be up to 80 mg/day.

## Tablets

- **Ritalin:** 5, 10 or 20 mg tablets
- **Ritalin SR (sustained release):** 20 mg sustained release tablets
- **Methylin:** 5, 10 or 20 mg tablets
- **Methylin ER (extended release):** 5, 10 or 20 mg extended release tablets
- **Metadate ER:** 10 or 20 mg controlled release tablets
- **Equasym:** 5, 10, 20 or 30 mg tablets
- **Rubifen:** 5, 10 or 20 mg tablets
- **Motiron:** 5, 10 or 20 mg tablets

- **Stimdate:** 10 mg tablets
- **Attenta:** 10 mg tablets

### Capsules

- **Concerta:** 18, 27, 36, and 54 mg osmotic controlled release capsules (patented until 2018)
  Note: Some adults may take two 36 mg capsules for an effective dose of 72 mg
- **Ritalin LA (long acting):** 10, 20, 30 or 40 mg controlled release capsules
- **Metadate CD (controlled dose):** 10, 20, 30, 40, 50 or 60 mg controlled release capsules
- **Biphentin:** 10, 15, 30, 40, or 60 mg suspended release capsules

Concerta pills are marked with the letters "ALZA" and followed by: "18", "27", "36", or "54", relating to the (mg) dosage strength. Approximately 22% of the Concerta dose is immediate release, and the remaining 78% of the dose is evenly released over 10-12 hours post ingestion.

Ritalin LA capsules are marked with the letters "NVR" (abbrev.: Novartis) and followed by: "R20", "R30", or "R40", depending on the (mg) dosage strength. The capsules contain two types of beads; 50% of the beads are immediate release, and the other 50% of the beads are enteric-coated, designed to give a second delayed release approximately 5 hours post ingestion.

Metadate CD capsules are marked with the letters "UCB" and followed by: "579, 10mg"; "580, 20mg"; "581, 30mg"; "582, 40mg"; "583, 50mg"; or "584, 60mg". The capsules contain two types of beads; 30% of the beads are immediate release, and the other 70% of the beads are evenly sustained release over approximately 8 hours.

### Patches

- **Daytrana** 10, 15, 20 or 30 mg controlled release patches (1.1, 1.6, 2.2 or 3.3 mg/hour for 9 hours)

## *Adverse effects*

Some adverse effects may emerge during chronic use of methylphenidate so a constant watch for adverse effects is recommended. Some adverse effects of stimulant therapy may emerge during long-term therapy, but there is very little research of the long-term effects of stimulants. The most common side effects of methylphenidate are nervousness and insomnia or drowsiness. Other adverse reactions include:

- Abdominal pain
- Akathisia
- Alopecia
- Angina

- Appetite loss
- Anxiety or panic attacks
- Blood pressure and pulse changes (both up and down)
- Cardiac arrhythmia
- Diaphoresis (sweating)
- Dizziness
- Dyskinesia
- Headaches
- Hypersensitivity (including skin rash, urticaria, fever, arthralgia, exfoliative dermatitis, erythema multiforme, necrotizing vasculitis, and thrombocytopenic purpura)
- Lethargy
- Nausea
- Palpitations
- Pupil dilation
- Short-term weight loss
- Somnolence
- Stunted growth
- Tachycardia
- Xerostomia (dry mouth aka cotton mouth)

## Known or suspected risks to health

Researchers have also looked into the role of methylphenidate in affecting stature, with some studies finding slight decreases in height acceleration. Other studies indicate height may normalize by adolescence. In a 2005 study, only "minimal effects on growth in height and weight were observed" after 2 years of treatment. "No clinically significant effects on vital signs or laboratory test parameters were observed."

A 2003 study tested the effects of dextromethylphenidate (Focalin), levomethylphenidate, and (racemic) dextro-, levomethylphenidate (Ritalin) on mice to search for any carcinogenic effects. The researchers found that all three preparations were non-genotoxic and non-clastogenic; d-MPH, d, l-MPH, and l-MPH did not cause mutations or chromosomal aberrations. They concluded that none of the compounds present a carcinogenic risk to humans. Current scientific evidence supports that long-term methylphenidate treatment does not increase the risk of developing cancer in humans.

It was documented in 2000, by Zito et al. "that at least 1.5% of children between the ages of two and four are medicated with stimulants, anti-depressants and anti-psychotic drugs, despite the paucity of controlled scientific trials confirming safety and long-term effects with preschool children."

On March 22, 2006, the FDA Pediatric Advisory Committee decided that medications using methylphenidate ingredients do not need black box warnings about their risks, noting that "for normal children, these drugs do not appear to pose an obvious cardiovascular risk." Previously, 19 possible cases had been reported of Cardiac arrest

linked to children taking methylphenidate and the Drug Safety and Risk Management Advisory Committee to the FDA recommend a "black-box" warning in 2006 for stimulant drugs used to treat attention deficit/hyperactivity disorder.

Doses prescribed of stimulants above the recommended dose level is associated with higher levels of psychosis, substance misuse and psychiatric admissions.

## Long-term effects

The effects of long-term methylphenidate treatment on the developing brains of children with ADHD is the subject of study and debate. Although the safety profile of short-term methylphenidate therapy in clinical trials has been well established, repeated use of psychostimulants such as methylphenidate is less clear. There are no well defined withdrawal schedules for discontinuing long-term use of stimulants. There is limited data that suggests there are benefits to long-term treatment in correctly diagnosed children with ADHD, with overall modest risks. Short-term clinical trials lasting a few weeks show an incidence of psychosis of about 0.1%. A small study of just under 100 children that assessed long-term outcome of stimulant use found that 6% of children became psychotic after months or years of stimulant therapy. Typically, psychosis would abate soon after stopping stimulant therapy. As the study size was small, larger studies have been recommended. The long-term effects on mental health disorders in later life of chronic use of methylphenidate is unknown. Concerns have been raised that long-term therapy might cause drug dependence, paranoia, schizophrenia and behavioral sensitisation, similar to other stimulants. Psychotic symptoms from methylphenidate can include, hearing voices, visual hallucinations, urges to harm oneself, severe anxiety, euphoria, grandiosity, paranoid delusions, confusion, increased aggression and irritability. Methylphenidate psychosis is unpredictable in whom it will occur. Family history of mental illness does not predict the incidence of stimulant toxicosis in children with ADHD. High rates of childhood stimulant use is found in patients with a diagnosis of schizophrenia and bipolar disorder independent of ADHD. Individuals with a diagnosis of bipolar or schizophrenia who were prescribed stimulants during childhood typically have a significantly earlier onset of the psychotic disorder and suffer a more severe clinical course of psychotic disorder. Knowledge of the effects of chronic use of methylphenidate is poorly understood with regard to persisting behavioral and neuroadaptational effects.

Tolerance and behavioural sensitisation may occur with long-term use of methylphenidate. There is also cross tolerance with other stimulants such as amphetamines and cocaine. Stimulant withdrawal or rebound reactions can occur and should be minimised in intensity, e.g. via a gradual tapering off of medication over a period of weeks or months. A very small study of abrupt withdrawal of stimulants did suggest that withdrawal reactions are not typical. Nonetheless, withdrawal reactions may still occur in susceptible individuals. The withdrawal or rebound symptoms of methylphenidate can include psychosis, depression, irritability and a temporary worsening of the original ADHD symptoms. Methylphenidate due to its very short elimination half life may be more prone to rebound effects than d-amphetamine. Up to a

third of children with ADHD experience a rebound effect when methylphenidate dose wears off.

## Contraindications

Methylphenidate should not be prescribed concomitantly with tricyclic antidepressants, such as desipramine, or monoamine oxidase inhibitors, such as phenelzine or tranylcypromine, as methylphenidate may dangerously increase plasma concentrations, leading to potential toxic reactions (mainly, cardiovascular effects). Methylphenidate should not be prescribed to patients who suffer from severe arrhythmia, hypertension or liver damage. It should not be prescribed to patients who demonstrate drug-seeking behaviour, pronounced agitation or nervousness. Care should be taken while prescribing methylphenidate to children with a family history of Paroxysmal Supraventricular Tachycardia (PSVT).

## Special precautions

Special precaution is recommended in individuals with epilepsy with additional caution in individuals with uncontrolled epilepsy due to the potential for methylphenidate to lower the seizure threshold.

## Pregnancy

The U.S. Food and Drug Administration (FDA) gives methylphenidate a pregnancy category of C, and women are advised to only use the drug if the benefits outweigh the potential risks. Not enough animal and human studies have been conducted to conclusively demonstrate an effect of methylphenidate on fetal development. In 2007, empirical literature included 63 cases of prenatal exposure to methylphenidate across three empirical studies. One of these studies (N = 11) demonstrated no significant increases in malformations. A second (N = 13) demonstrated one major malformation in newborns with early exposure to methylphenidate, which was in the expected range of malformations. However, this was a cardiac malformation, which was not within the statistically expected range. Finally, in a retrospective analysis of patients' medical charts (N = 38), researchers examined the relationship between *abuse* of intravenous methylphenidate and pentazocine in pregnant women. Twenty-one percent of these children were born prematurely, and several had stunted growth and withdrawal symptoms (31% and 28%, respectively). Intravenous methylphenidate abuse was confounded with the concurrent use of other substances (e.g., cigarettes, alcohol) during pregnancy.

## Overdose

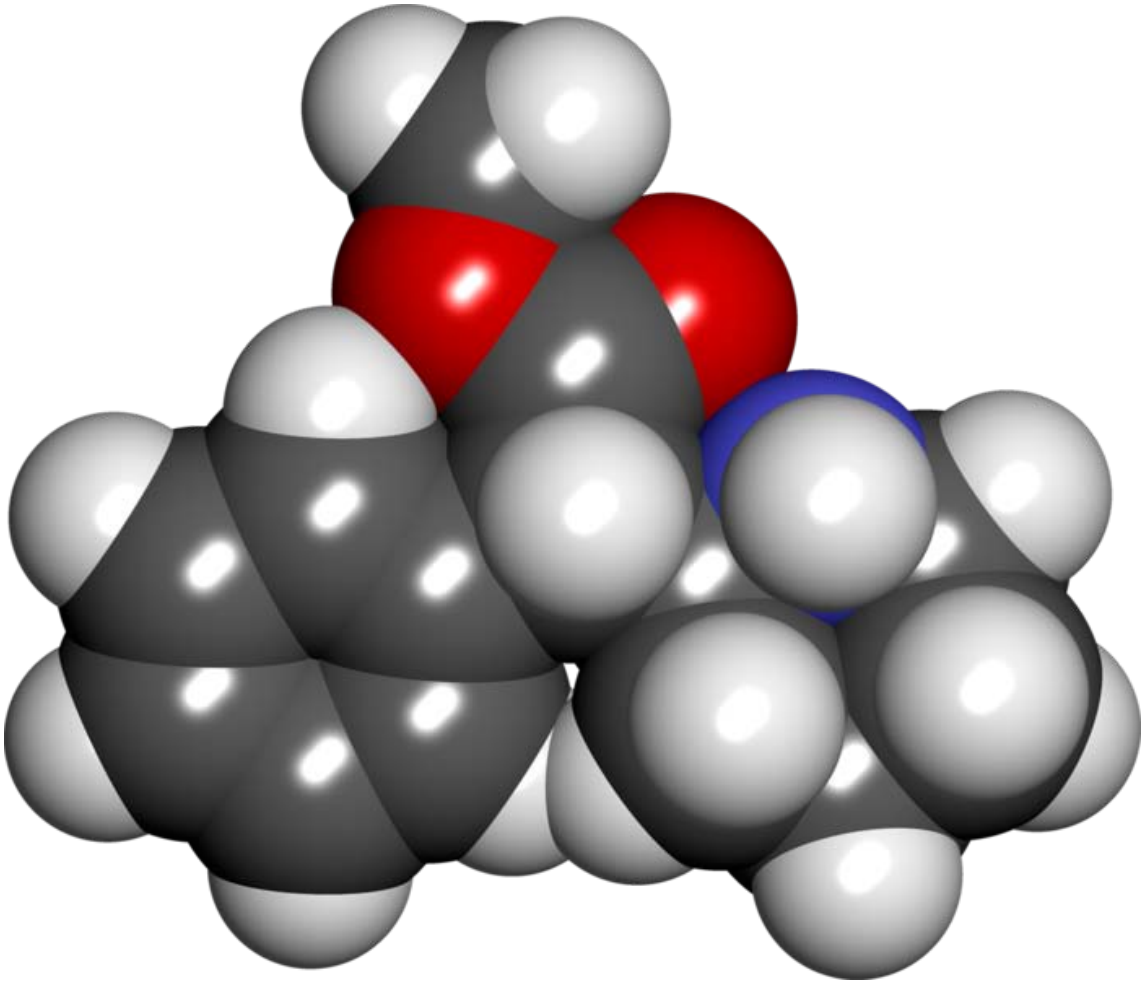
In 2004, over 8000 methylphenidate ingestions were reported in US poison center data. The most common reasons for intentional exposure were drug abuse and suicide attempts. An overdose manifests in agitation, hallucinations, psychosis, lethargy, seizures, tachycardia, dysrhythmias, hypertension, and hyperthermia. Benzodiazepines

may be used as treatment if agitation, dystonia, or convulsions are present. MPH is prescribed at 1/100th of the estimated lethal dose.

## *Detection in biological fluids*

The concentration of methylphenidate or ritalinic acid, its major metabolite, may be quantified in plasma, serum or whole blood in order to monitor compliance in those receiving the drug therapeutically, to confirm the diagnosis in potential poisoning victims or to assist in the forensic investigation in a case of fatal overdosage.

## *Pharmacology*



3d space filling model of methylphenidate

Methylphenidate is a chain substituted amphetamine derivative. Similar to amphetamines and cocaine, a keCite journal|author=Iversen L |title=Neurotransmitter transporters and their impact on the development of psychopharmacology |journal=British Journal of Pharmacology |volume=147 |issue=Suppl 1 |pages=S82–8 |year=2006 |month=January |pmid=16402124 |pmc=1760736 |doi=10.10 Methylphenidate has both DAT and NET

binding affinity, with the dextromethylphenidate enantiomers displaying a prominent affinity for the norepinephrine transporter. Both the dextro- and levorotary enantiomers displayed receptor affinity for the serotonergic $5HT_{1A}$ and $5HT_{2B}$ subtypes, though direct binding to the serotonin transporter was not observed.

The enantiomers and the relative psychoactive effects and CNS stimulation of dextro- and levo-methylphenidate is analogous to what is found in amphetamine, where dextro-amphetamine is considered to have a greater psychoactive and CNS stimulatory effect than levo-amphetamine.

## Pharmacodynamics

Methylphenidate exerts its therapeutic effects via blocking the reuptake of dopamine into nerve terminals (as well as stimulating the release of dopamine from dopamine nerve terminals) resulting in increased dopamine levels in the synapse. The onset of central nervous system effects occurs rapidly after intake of methylphenidate and persist for about 4 hours. The mechanism of action is comparable with that of cocaine with usual doses of both drugs occupying 50% of dopamine transporters. However, effects such as euphoria that resembles that of cocaine are rare at doses prescribed clinically.

The means by which methylphenidate affects people diagnosed with ADHD are not well understood. Some researchers have theorized that ADHD is caused by a dopamine imbalance in the brains of those affected. Methylphenidate is a norepinephrine and dopamine reuptake inhibitor, which means that it increases the level of the dopamine neurotransmitter in the brain by partially blocking the dopamine transporter (DAT) that removes dopamine from the synapses. This inhibition of DAT blocks the reuptake of dopamine and norepinephrine into the presynaptic neuron, increasing the amount of dopamine in the synapse. It also stimulates the release of dopamine and norepinephrine into the synapse. Finally, it increases the magnitude of dopamine release after a stimulus, increasing the salience of stimulus. An alternate explanation that has been explored is that the methylphenidate affects the action of serotonin in the brain. However, benefits with other stimulants that have a different mechanism of action indicates that support for a deficit in specific neurotransmitters is unsupported and unproven by the evidence and remains a speculative hypothesis.

It is commonly asked why a stimulant should be used to treat hyperactivity, which seems paradoxical. However, MRIs of ADHD brains previously drugged with stimulants show decreased activity in the brain centers critical to concentration and impulse control.

One study finds that methylphenidate reduces the increases in brain glucose metabolism during performance of a cognitive task by about 50%. This suggests that, similar to increasing dopamine and norepinephrine in the striatum and prefrontal cortex, methylphenidate may focus activation of certain regions and make the brain more efficient. This is consistent with the observation that stimulant drugs can enhance attention and performance in some individuals. If brain resources are not optimally distributed (for example, in individuals with ADHD or sleep deprivation), improved

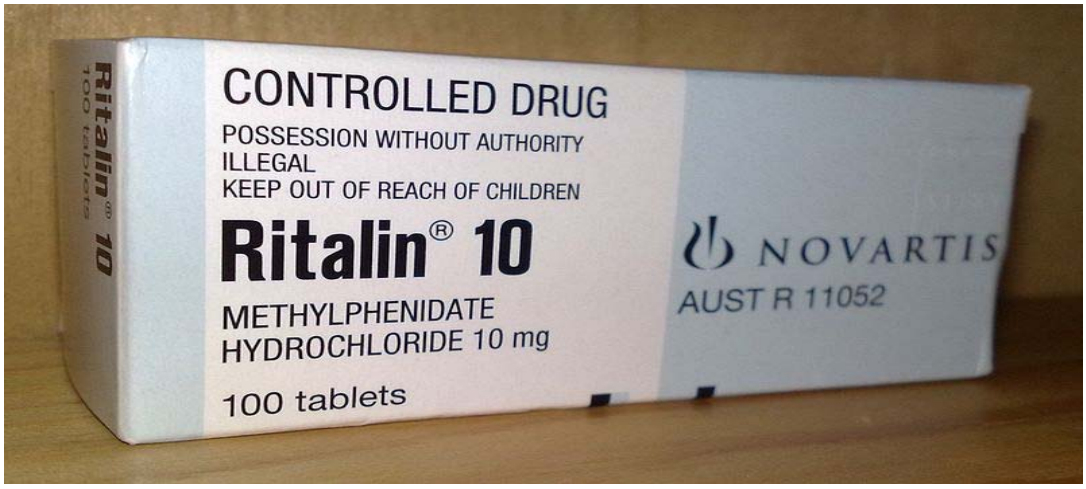
performance could be achieved by reducing task-induced regional activation. Stimulant delivery when brain resources are already optimally distributed may then adversely affect performance.

A paper published in *Biological Psychiatry* reports that methylphenidate fine-tunes the functioning of neurons in the prefrontal cortex - a brain region involved in attention, decision-making and impulse control - while having few effects outside it. The team studied PFC neurons in rats under a variety of methylphenidate doses, including one that improved the animals' performance in a working memory task of the type that ADHD patients have trouble completing. Using microelectrodes, the scientists observed both the random, spontaneous firings of PFC neurons and their response to stimulation of the hippocampus. When they listened to individual PFC neurons, the scientists found that while cognition-enhancing doses of methylphenidate had little effect on spontaneous activity, the neurons' sensitivity to signals coming from the hippocampus increased dramatically. Under higher, stimulatory doses, on the other hand, PFC neurons stopped responding to incoming information.

## *Interactions*

Intake of adrenergic agonist drugs or pemoline with methylphenidate increases the risk of liver toxicity. Antidepressants taken in conjunction with methylphenidate may cause hypertension, hypothermia and convulsions. When methylphenidate is coingested with ethanol, a metabolite called ethylphenidate is formed via hepatic transesterification, not unlike the hepatic formation of cocaethylene from cocaine and alcohol. Coingestion of alcohol (ethanol) also increases the blood plasma levels of d-methylphenidate by up to 40%. It is more selective to the dopamine transporter (DAT) than methylphenidate, having approximately the same efficacy as the parent compound, but has significantly less activity on the norepinephrine transporter (NET).

## *Abuse potential*




Legal warning printed on Ritalin carton (AU)

Methylphenidate has high potential for abuse and addiction due to its pharmacological similarity to cocaine and amphetamines. Methylphenidate, like other stimulants, increases dopamine levels in the brain, but at therapeutic doses this increase is slow, and thus euphoria does not typically occur except in rare instances. The abuse potential is increased when methylphenidate is crushed and insufflated (snorted), or when it is injected, producing effects almost identical to cocaine. Cocaine-like effects can also occur with very large doses taken orally. The dose, however, that produces euphoric effects varies between individuals. Methylphenidate is actually more potent than cocaine in its effect on dopamine transporters. Methylphenidate should not be viewed as a weak stimulant as has previously been hypothesised.

The primary source of methylphenidate for abuse is diversion from legitimate prescriptions, rather than illicit synthesis. Those who use it to stay awake do so by taking it orally, while intranasal and intravenous are the preferred means for inducing euphoria. IV users tend to be adults whose use may cause panlobular pulmonary emphysema.

Abuse of prescription stimulants is higher amongst college students than non-college attending young adults. College students use methylphenidate either as a study aid or to stay awake longer. Increased alcohol consumption due to stimulant misuse has additional negative effects on health. Methylphenidate's pharmacological effect on the central nervous system is almost identical to that of cocaine. Studies have shown that the two drugs are nearly indistinguishable when administered intravenously to cocaine addicts.

However, cocaine has a slightly higher affinity for the dopamine receptor in comparison to methylphenidate, which is thought to be the mechanism of the euphoria associated with the relatively short-lived cocaine high. Reports of users experimenting with mixing methylphenidate with caffeine and benzocaine to produce a powder for insufflation (snorting) for an even more cocaine-like effect began to appear in the middle 1970s; this is apparently an incrementation upon a mixture known as Toot containing phenylpropanolamine, caffeine, and benzocaine in the search for legal highs. As moderate doses of cocaine have caffeine-like effects and benzocaine produces a slight stimulant effect of its own perhaps 5 per cent the strength of cocaine with a ceiling in that range, the mixture is reported to have at least some of the sought-after effects.

Patients who have been prescribed Ritalin have been known to sell their tablets to others who wish to take the drug recreationally. In the UK it has been dubbed "kiddie coke" due to its low price and high availability amongst young people. In the USA it is one of the top ten stolen prescription drugs and is known as "Vitamin R" and "The R Ball". Recreational users may crush the tablets and either snort the powder, or dissolve the powder in water, filter it through cotton wool into a syringe to remove the inactive ingredients and other particles and inject the drug intravenously. Both of these methods increase bioavailability and produce a much more rapid onset of effects than when taken orally (within c.5–10 minutes through insufflation and within just 10–15 seconds through intravenous injection); however the overall duration of action tends to be decreased by any non-oral use of drug preparations made for oral use.

Methylphenidate is sometimes used by students to enhance their mental abilities, improving their concentration and helping them to study. Professor John Harris, an expert in bioethics has said that it would be unethical to stop healthy people taking the drug. He also argues that it would be "not rational" (i.e. irrational) and against human enhancement to not use the drug to improve people's cognitive abilities. Professor Anjan Chatterjee however has warned that there is a high potential for abuse and may cause serious adverse effects on the heart, meaning that only people with an illness should take the drug. In the *British Medical Journal* he wrote that it was premature to endorse the use of Ritalin in this way as the effects of the drug on healthy people have not been studied. Professor Barbara Sahakian has argued that the use of Ritalin in this way may give students an unfair advantage in examinations and that as a result universities may have to consider making students give urine samples to be tested for the drug.

## *Legal status*

- Israel Over The Counter: February 9th 2011 The Ethics Committee of the Medical Histadrut (Federation) will now be permitted to sell the psycho-stimulant drug that treats attention-deficit hyperactivity disorder (ADHD) Ritalin (Methylphenidate) without a doctor's prescription.

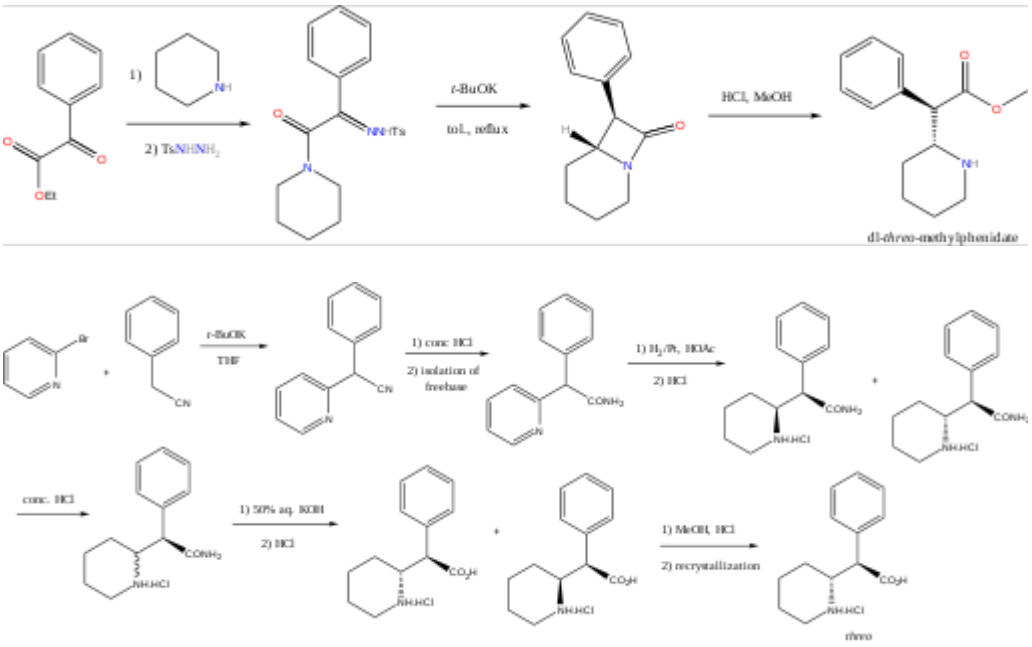
Professor Esther Shohami, a lecturer and researcher in the pharmacological department in the Hebrew University's Faculty of Medicine, is critical of the decision.

- Internationally, methylphenidate is a Schedule II drug under the Convention on Psychotropic Substances.
- In the United States, methylphenidate is classified as a Schedule II controlled substance, the designation used for substances that have a recognized medical value but present a high likelihood for abuse because of their addictive potential.
- In the United Kingdom, methylphenidate is a controlled 'Class B' substance, and possession without prescription is illegal, with a sentence up to 14 years and/or an unlimited fine.
- In New Zealand, it is a 'class B2 controlled substance'. Unlawful possession is punishable by six-month prison sentence and distribution of it is punishable by a 14-year sentence.

## *Chemistry of MPH*

Four isomers of methylphenidate are known to exist. One pair of threo isomers and one pair of erythro are distinguished, from which only d-threo-methylphenidate exhibits the pharmacologically usually desired effects. When the drug was first introduced it was sold as a 3:1 mixture of erythro:threo diastereomers. The erythro diastereomers are also *pressor* amines. "TMP" is referring only to the threo product that does not contain any erythro diastereomers. Since the threo isomers are energetically favored, it is easy to epimerize out any of the undesired erythro isomers. The drug that contains only dextrorotary methylphenidate is called d-TMP. A review on the synthesis of

enantiomerically pure ("*R*,2'*R*)-(+)-*threo*-methylphenidate hydrochloride has been published.




Satendra Singh (2000), pages 81–7.

## *Controversy*

Methylphenidate has been the subject of controversy in relation to its use in the treatment of ADHD. One such criticism is prescribing psychostimulants medication to children to reduce ADHD symptoms. Calls have been made that methylphenidate be severely restricted in its use. The pharmacological effects of methylphenidate are almost identical to cocaine and amphetamines, which is the desired effect in the treatment of ADHD, and how methylphenidate works.

The abuse pattern of methylphenidate is very similar to heroin and amphetamines. A 2002 study showed that rats treated with methylphenidate are more receptive to the reinforcing effects of cocaine. The contention that methylphenidate acts as a gateway drug has been discredited by multiple sources, abuse is statistically very low, and that "stimulant therapy in childhood does not increase the risk for subsequent drug and alcohol abuse disorders later in life".

Another controversial idea surrounding ADHD is that a group of ADHD children have, in general, healthy brains with no gross neurological deficits. This concept, however, is seen as outdated by a few scientists in current medical research, who claim they can identify an ADHD child's brain using CT brain scans, and how methylphenidate interacts with it. The problem herein being that no control was used in the cited research that would differentiate an ADHD child's brain from one that had been treated with stimulants

beforehand. As a result, the aforementioned research of CT brain scans of previously drugged children with ADHD is biased with insignificant findings.

Treatment of ADHD by way of Methylphenidate has led to legal actions including malpractice suits regarding informed consent, inadequate information on side effects, misdiagnosis, and coercive use of medications by school systems. Methylphenidate has been tested extensively in the U.S. on children by the FDA, with ongoing research into the drug. In the U.S. and the United Kingdom, it is approved for use in children and adolescents. The FDA recently approved the use of methylphenidate for use in treating adult ADHD. Methylphenidate has been approved for adult use in the treatment of narcolepsy."