BAP consensus guidelines on autism spectrum disorder

STEVE CHAPLIN

The British Association for Psychopharmacology (BAP) recently issued new guidelines on the assessment and treatment of autism spectrum disorder, based on consensus rather than systematic review. This article provides an overview of the main recommendations.

Autism spectrum disorder (ASD) has a lifetime prevalence of about 1%. Assessment and management is complex; over one-quarter of people with ASD (and rising) are treated with psychotropic medication even though many are concerned about adverse effects and lack of effectiveness. Some people with ASD don’t want medication for their core symptoms, making individualised management essential.

This is a state of affairs in which comprehensive guidance would be useful, the British Association for Psychopharmacology (BAP) concluded, so it convened a meeting of psychiatrists, psychologists, researchers and service user representatives to review the assessment and management of ASD in children, adolescents and adults. A literature review provided evidence to support the consensus points that emerged, which the group then revised to formulate the guideline. The resulting guidance, published in January 2018, is a document based on consensus, not systematic review, that addresses all aspects of ASD and its management from aetiology to service provision.¹

NICE published its guidance on diagnosis and management of ASD in the under-19s in 2011 and 2013 and in adults in 2012 with partial updates in 2016 and 2017.²⁻⁴ The BAP occasionally refers to this guidance in its own document but (with the exception of service provision) does not explain how the two guidelines should be implemented jointly.

Aetiology

ASD has about 80% heritability with 10–15% of cases associated with monogenic syndromes such as Fragile X syndrome. But the genetic risk is due to multiple polymorphisms of small effect and the identified variants affect a number of neurobiological pathways, including NMDA and GABA receptors and...
microglial activation, and the nature of their impact is not well understood. Some of these pathways are also affected by environmental risk factors, which include significant prematurity, perinatal hypoxia, maternal pre-/perinatal infections, materna! vitamin D deficiency, higher paternal age, gestational valproate exposure, maternal obesity and very low birthweight (<1500g).

The neurodevelopmental picture of ASD is complex. Structural differences in the brain may be evident early in life and some individuals may have early brain overgrowth that later slows, with brain size becoming similar to average by the age of 10–15 years. Abnormalities in serotonin, excitatory glutamate and inhibitory GABA systems, and the oxytocin system have been identified. The balance of excitatory and inhibitory stimuli appears to be altered but, though consistent with preclinical models of ASD, this is not unique to ASD and varies according to the cell type and brain region studied. Oxytocin, which regulates social bonding and recognition, has a regulatory role on prenatal excitatory/inhibitory balance and may continue to do so after birth. Dysfunction of microglial cells, caused by genetic mutations or environmental factors, could also alter brain development and function and contribute to the pathogenesis of ASD.

**Diagnosis and assessment**
The American Psychiatric Association’s Diagnostic and Statistical Manual of Mental Disorders (DSM-5) replaced the term ‘autism’ with ASD, acknowledging the blurred neurobiological distinctions between the different subtypes, and does not specify age at onset. The BAP recommends considering using DSM-5 criteria because they enable a diagnosis of ASD in adults and a diagnosis of other co-current disorders. Diagnosis is a multidisciplinary, multistage and challenging process. ASD symptoms may be obscured by a psychiatric disorder, core symptoms manifest differently in men and women, and adults develop adaptive behaviours to manage social situations. The guideline provides tables of the instruments most frequently used when assessing children and adults, and recommends familiarity with their pros and cons.

**Psychiatric disorders**
Almost 80% of people with ASD develop at least one psychiatric disorder (about twice the frequency in the general population). In children, 85% experience irritability, self-injurious behaviour and temper tantrums; about half have an anxiety disorder (most often specific phobia or social phobia). Many children meet diagnostic criteria for attention deficit hyperactivity disorder (ADHD) (28–53%) or oppositional defiant disorder or conduct disorder (7–37%). Sleeping problems

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<th>Anxiety disorders</th>
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<td>Consider a cautious trial of an SSRI followed by risperidone if poor response. Monitor for worsening of anxiety in some children (B)</td>
<td>Decision on treatment needs to be made on a case-by-case basis Follow the BAP guidelines for treating anxiety (S)</td>
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<td>Melatonin, if possible, in combination with a behavioural intervention (A) Prolonged use of benzodiazepines and related GABA agonists is not recommended (S)</td>
<td>Melatonin, if possible, in combination with a behavioural intervention (extrapolation from findings in children) (S) Prolonged use of benzodiazepines and related GABA agonists is not recommended (S)</td>
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<th>Irritability</th>
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<td>Risperidone or aripiprazole but only when behavioural or educational approaches have failed (A)</td>
<td>Decision on treatment needs to be made on a case-by-case basis Aripiprazole or risperidone or an SSRI should only be considered cautiously and after considering alternatives (S)</td>
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<td>First line: methylphenidate Second line: atomoxetine, or alpha2A receptor agonist Children with ASD may experience more side-effects and show less response than non-ASD patients with ADHD (A)</td>
<td>Decision on treatment needs to be made on a case-by-case basis Follow the BAP guidelines for treating ADHD (S)</td>
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<th>Tic disorders and Tourette syndrome</th>
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<td>Decision on treatment needs to be made on a case-by-case basis (S)</td>
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ADHD = attention deficit/hyperactivity disorder; ASD = autism spectrum disorder; BAP = British Association for Psychopharmacology; GABA = gamma-aminobutyric acid; SSRI = selective serotonin re-uptake inhibitor

Evidence rated A to D using the criteria by Shekelle et al. (1999), with grade A indicating the recommendation is supported by the highest quality evidence. The category S corresponds to a standard for clinical care, which comprises a consensus on good clinical practice in the absence of other evidence.

**Table 1.** British Association for Psychopharmacology (BAP) consensus recommendations for the pharmacological treatment of co-occurring conditions and symptoms in children and adults with autism spectrum disorder (ASD)
Autism spectrum disorder

Affect 50–80% of children, though it’s unclear whether this is due primarily to ASD or the associated conditions. Adults often have mood disorder (lifetime prevalence 26–57%) and ADHD (11–43%), though psychiatric diagnoses (especially social phobia) are less common than among children. About one-fifth of adults and children have a tic disorder.

“Identifying and treating co-occurring disorders in adults with ASD is critical,” the BAP states, because they have “a marked impact on functional impairment and caregiver burden, comparable to that reported by persons caring for individuals with a brain injury.”

Pharmacological treatment

Core symptoms

BAP summarises the findings of clinical trials of SSRIs, dopamine antagonists, glutamatergic agonists, GABAergic agonists, methylphenidate and oxytocin. It concludes that there is no clear evidence of efficacy to support the routine use of any agent for core symptoms of ASD. The atypical antipsychotics risperidone and aripiprazole have been shown to be helpful in the treatment of repetitive behaviours but the balance of risk and benefit of treatment requires careful assessment and regular re-evaluation.

Co-occurring conditions and symptoms

The BAP recommendations for drug treatment for conditions and symptoms co-occurring with ASD in adults and children are summarised in Table 1.

Treatment in children

SSRIs are widely prescribed for people with ASD but no rigorous trials have evaluated them in children, who are more sensitive to their adverse effects. They should be used in low doses, titrated gradually and carefully monitored. In children with anxiety or obsessive compulsive disorder (OCD), the evidence supporting the use of risperidone, clomipramine and the SSRIs is weak and their effects are of uncertain clinical significance. The BAP recommends following its 2014 guideline on treating OCD and anxiety.

By contrast, melatonin is effective in sleep disorder: it reduces sleep latency and increases sleep duration, though it may not reduce nocturnal wakening and earlier wakening may occur. The combination of melatonin and cognitive behavioural therapy (CBT) is more effective than either intervention alone. Melatonin is well tolerated, with minimal or no adverse effects.

Irritability (including severe tantrums, aggression or self-injury) is more common in individuals with ASD who also have a mood or anxiety disorder, and treatment for these conditions should be considered in the management of irritability. There is some evidence that risperidone and aripiprazole are at least moderately effective...
in treating irritability but the balance of risk and benefit of treatment should be weighed carefully and behavioural and educational interventions should be considered first. If an antipsychotic is prescribed, progress should be monitored against a treatment target, and the BAP recommends periodically trying to reduce the dose and discontinue treatment to determine whether treatment is still needed. Of the other treatments investigated for irritability, arbaclofen and amantadine are not recommended and further trials are needed to confirm the possible benefit of minocycline.

There is good evidence to support the use of methylphenidate for co-occurring ADHD in children with ASD; atomoxetine is “a good alternative” offering equal efficacy, especially when combined with parent training. When these agents are unsuitable, alpha2a-receptor agonists (clonidine, guanfacine and lofexidine) are a further option. Limited evidence suggests that risperidone and aripiprazole are slightly less effective and carry a higher risk of adverse effects but they may be useful if closely monitored.

**Treatment in adults**

Evidence to support the role of drug therapy in adults with ASD is even more sparse than for children. SSRIs appear to be well tolerated but offer only modest benefits in adults with ASD and anxiety disorders, predominantly OCD; there is insufficient evidence to support the use of risperidone. The BAP therefore recommends cautiously following its guideline on anxiety.5

There are no trials of melatonin in adults with ASD but by extension of evidence in children and in adults without ASD, the BAP recommends cautiously following its guidelines on sleep disorders.7 Melatonin is safe enough to justify an early trial but prolonged use of benzodiazepines and related GABA agonists is not recommended due to the risk of tolerance and adverse effects.

Behavioural approaches should be tried before risperidone or other antipsychotics to treat irritability. Pregnenolone, a steroid precursor present in the brain, has been shown to improve irritability in one small trial but further studies are needed.

There are no trials of treatments for ADHD in adults with ASD; once more, cautious use of the relevant BAP guideline6 is recommended. There are no studies of treatment for tic disorders in people with ASD and the decision to prescribe should be made on a case by case basis.

**Non-pharmacological approaches for core ASD symptoms**

The BAP states that full analysis of psychosocial interventions for children with ASD is outside the scope of its guideline but it nonetheless offers advice. It recommends a specific social-communication intervention appropriate to developmental level for adolescents and children, and social skills training for adolescents. Exclusion diets, secretin, chelation and hyperbaric oxygen therapy should not be used.

Adults with ASD should be offered behavioural training programmes to develop the life skills they need, such as using public transport, having a job and using leisure facilities, focusing on supporting access to community activities and increasing quality of life. Adults with social interaction problems should be considered for a group or individual social-learning programme but facilitated communication is not recommended.

**Service provision**

In 2011, NICE guidance recommended the development of multigateway teams for children and adolescents with ASD. However, implementation of this guideline is variable and often weighted towards diagnosis rather than treatment and support, leaving “unmet needs around common co-existing conditions including feeding problems, sleep problems, anxiety, hyperactivity and sensory problems.” The BAP reviews what evidence there is on service provision for people with ASD but acknowledges its guideline but it nonetheless offers advice. It recommends a specific social-communication intervention appropriate to developmental level for adolescents and children, and social skills training for adolescents. Exclusion diets, secretin, chelation and hyperbaric oxygen therapy should not be used.

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**The future**

The single thread running throughout the guideline is the absence of quality evidence from clinical trials. The BAP would like to see better-designed studies – larger, longer, using biomarkers, and with better evaluation of safety – to evaluate interventions in populations more representative of the people using NHS services. In particular, studies are needed in children under five years old – a time when, the BAP believes, brain plasticity is at its greatest and interventions could have the most dramatic effect.

In the past, trials have excluded people with ASD who have intellectual disabilities, though over one-third are affected in this way. Novel trial designs will be needed to address these shortcomings. There is also a need for further trials on the effectiveness of social-communication interventions, applied behaviour analysis, behaviourally-based life skills training and anti-victimisation CBT. Service models should be assessed using patient experience and functional measures as outcomes.

**Summary**

The BAP is in close agreement with NICE that drug treatment is not appropriate for core symptoms of ASD, that psychosocial...
interventions are preferred to drugs, and that drug treatment should be regularly reviewed. But while NICE confines its recommendations to the here and now, the BAP is more open to treatments that appear to show promise. For example, NICE accepts a role for drug treatment to aid sleep but does not mention melatonin, whereas the BAP is more supportive of this approach.

The BAP says its recommendations are based on the current literature and expert opinion. Its review is “not intended to be exhaustive, but to highlight key findings and also place them in a clinical context, drawing from the practical experience of the contributors.” This approach should help the clinician “to place the evidence and our recommendations in the individual context of the person with ASD in front of them.”

References

Declaration of interests
None to declare.

Steve Chaplin is a medical writer specialising in therapeutics